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# MIXED TUMORS OF THE KIDNEY IN INFANCY AND CHILDHOOD

## A STUDY OF SEVENTEEN CASES[1]

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THIS paper is based upon a study of 17 cases of malignant tumors of the kidney which occurred in infants and children. Some of the patients were under our personal observation and some of them were on the services of others at the Children's Memorial Hospital and the Presbyterian Hospital of Chicago, and we were given the opportunity of studying the pathological specimens removed from such cases.

An interesting fact brought out in our study was that, in many instances, the true nature of the tumor was not recognized either at the time of operation or at the time the histological examination was made. For example, a review of the case histories showed the following histopathological diagnoses: multiple cell type sarcoma, myxomatous tumor, alveolar round cell sarcoma, myxomatous sarcoma, and, in one instance, hypernephroma. A careful histological study of these tumors, however, showed that the diagnoses made were not correct and that the tumors really belonged to the interesting group known as mixed tumors.

Malignant tumors of the kidney occurring in infants and children are rare, as may be seen from a review of the literature. Bugbee and Wollstein, in a review of 4,903 autopsies performed on infants and children, report no cases of malignant renal tumor. Lowsley and Butterfield, in a recent series in which they reported their findings in 100 cases of urological lesions in infants and children, mention no case of malignant tumor. Thomas and Birdsall, in an exhaustive report of their experiences in children, do not include any cases of malignant renal tumor, but Magoun and McCarty report finding malignant renal tumors in 7 children.

According to Thomas, in infants and children tumors of the pelvis of the kidney are rare as compared with the occurrence of tumors of the renal parenchyma. He reports a very interesting type of tumor of the kidney pelvis. Deming some time ago reported a case of congenital sarcoma in a child 29 days old. Hyman, in a series of 70 renal neoplasms, reported 10 cases of mixed tumors. Hasner recently reported 4 cases of mixed tumors of the kidney, 3 in infants and children and 1 in a man aged 45 years. Recently Wollstein reported a series of 18 cases of malignant tumors of the kidney in children; 17 of them were mixed tumors.

That, during infancy and childhood, malignant tumors occur in other organs is evident from a somewhat cursory review of the literature. Among recent articles dealing with this subject are the following: "Angiosarcoma of the Liver" (Bondy); "Primary Carcinoma of the Liver" (Castle); "Tumors of the Ovary"

[1] Read at the annual meeting of the American Association of Genito-Urinary Surgeons, French Lick, Indiana, May 22, 23, and 24, 1930.

(Downs); "Sarcoma of the Small Intestine" (Fullerton); "Carcinomatous Ovarian Teratoma" (Harris); "Sarcoma of the Bladder" (Mixter). Therefore, while the kidney is not the only organ that may be the seat of malignant disease in infancy and childhood, it is true that this organ is easily the most frequent site of malignant disease in the genito-urinary tract, and that the most common type of malignancy is the so-called mixed tumor of Wilms.

## REPORT OF CASES

A report of the 17 cases which form the basis of this study follows:

CASE 1. B. N., female, white, aged 1 year, was admitted to the Children's Memorial Hospital on the service of Dr. Joseph Brennemann, August 28, 1928, with the complaint that a mass was present on the left side of the abdomen. About 4 months previously, that is, when the child was 8 months old, the mother had noticed some distention of the left side of the abdomen. The mother stated that she did not think the child had lost weight but there was no gain in weight and her color was poor. There were no other symptoms.

Physical examination disclosed a fairly well nourished child, rather pale, with a prominent abdomen, and with heart and lungs negative. A very prominent, visible mass filled the entire left side of the abdomen. The mass extended from the arch of the ribs to the crest of the ilium and beyond the midline at the level of the umbilicus. It was smooth and firm and not tender. Temperature on admission to hospital was 100 degrees. Blood count: red blood cells, 3,000,000; white blood cells, 19,200; polymorphonuclear neutrophiles, 67 per cent; lymphocytes, 30 per cent; transitionals, 3 per cent. Urinalysis showed the urine clear; reaction, acid; albumin, 0; sediment, no blood cells and 30 pus cells per cubic millimeter. Cystoscopic examination showed the bladder to be normal. Ureteral catheters were passed without obstruction. The urine from the right kidney was normal; no urine was obtained from the left kidney. Roentgen-ray examination of the chest was negative. Pyelograms of the kidneys showed the right normal; the left, that no fluid entered the left pelvis.

Pre-operative diagnosis: malignant tumor of the left kidney.

*Operation.* (H. L. K.) September 28, 1928 (ether anæsthesia). The usual oblique kidney incision was made. A large, solid tumor of the kidney, about the size of the patient's head, was found. The veins covering the tumor were unusually large and tortuous. The surface was smooth; consistency firm; color gray. The tumor extended up under the costal arch above and into the iliac fossa below, and beyond the midline. Because of the size and fixation of the growth it was decided not to do a nephrectomy. Two pieces of tissue were removed for histological study.

Convalescence was uneventful. It was advised that the patient be given deep X-ray treatment.

The patient was admitted to the Presbyterian Hospital for deep roentgen-ray treatment and received, at the hands of Dr. C. B. Rose, 27 treatments. During the course of these treatments there was definite diminution in the size of the tumor, so that at the end of the course nephrectomy was advised.

December 5, 1928, therefore, the patient again entered the Children's Memorial Hospital.

General examination by Dr. Joseph Brennemann on January 7, 1929, gave no additional information, and no evidence of metastases. Dr. Brennemann concurred in the plan to carry out a nephrectomy. Blood count at this time showed red blood cells, 2,864,000; white blood cells, 13,400; hæmoglobin, 50 per cent. Urinalysis showed reaction, acid; albumin, trace; sugar, 0; 20 white blood cells per low power field; blood, 0.

Roentgen-ray examination of the chest was negative for evidences of metastasis. The temperature varied from 100 degrees to 101 degrees.

*Operation.* (H. L. K.) January 10, 1929 (ether anæsthesia), left nephrectomy. The tumor mass was freed with a great deal of difficulty because of the presence of adhesions. During the course of the dissection a rent in the diaphragm and a tear in the peritoneum occurred. The tear in the diaphragm was sewed with catgut and the opening in the peritoneum was closed with a running suture of catgut.

Convalescence was uneventful.

Histological diagnosis: adenomyosarcoma of the left kidney.

A recent examination revealed the presence of large tumor masses in the abdomen and roentgen-ray examination of the chest showed the presence of pulmonary metastases. The child died, May 18, 1929, 4 months after the nephrectomy. No autopsy was obtained.

*Description of specimen removed at operation.* The kidney and tumor mass together weighed 1,738 grams and measured 17 by 13½ by 14½ centimeters in maximum dimensions. The mass in general was oval. Its surface was smooth except for lobulation depressions of the tumor mass and for 12 nodulations of the surface, 3 of which were 2 centimeters in diameter, and the others 3 to 3.5 centimeters in diameter. The nodulations bulged outward from the central tumor mass and each was covered with a common capsule. The entire mass was firm. It flattened only slightly when placed on a hard table and was in general a gray to light brown. Delicate blood vessels only were present, and these were distended. In places the mass was dark red to brown, apparently because of old blood and new dark tissue.

Firmly attached to the upper pole was the remnant of this kidney. Grossly the kidney tissue was

Fig. 1. Case 1. Kidney and tumor removed surgically. Small remnant of kidney tissue. Slight dilatation of the kidney pelvis. Nodular surface of the tumor which in general outline is circular.

sharply defined, normally lobulated, dark brown, and its surface was flattened out so as to be continuous with the general contour of the mass. The total kidney substance present measured about 3.5 centimeters in diameter and weighed approximately 30 grams. Upon four transverse serial sections of the entire mass, the surfaces made by cutting were uniformly firm throughout all portions and consisted of clumps of tissue 3 to 4 centimeters in diameter, of a mottled gray to light brown, surrounded by narrow bands of densely rigid fibrous-like tissue. A center nodule was light yellow-brown, easily friable, and was evidently the result of pressure necrosis. Near the periphery of the mass at the lower pole there was a sharply defined dark brown spongy-porous nodule 3 centimeters in diameter. Nowhere was there any substance that was not cut easily by a sharp knife.

In histological sections of the tumor, the tissue consisted of densely packed cells which stained deeply. Although most of the cells were in clumps, many of them were arranged in bundles, that is, the nuclei were parallel, and about half of the cells had deep chromatin staining properties and the other cells were either diffusely granular, two to three times as long as they were wide, and many of them were vesicular. Between clumps of cells isolated eosinophilic polymorphonuclei were present. The nuclei that were vesicular were generally more spherical than oval. The cytoplasm generally was in strands and these stained pink and had transverse striations. Throughout the sections there were sharply defined tubular gland structures. These tubules in general were most abundant where the epithelial cells were densest. Nuclei of the tubular gland cells stained deeply; they were more oval than round and were situated in the mid-portion of the cell, which is semicolumnar in shape. In the lumen of the tubules the content was of non-cellular globoid structure and cell detritus. Where the tissue was less cellular, the nuclei were more spherical and here isolated lymphocytic polymorphonuclears were present. In the central portion the nuclei stain was faint, the cells were scanty, and the cytoplasm was grossly granular and stained poorly, as in pressure necrosis. Leucocytes were moderately abundant throughout, but in places they were present in clumps.

In sections stained with phosphotungstic acid hematoxylin, there were found dense striated muscle fibers in bundles. These fibers and bundles ramified throughout the epithelial cells masses, but were more

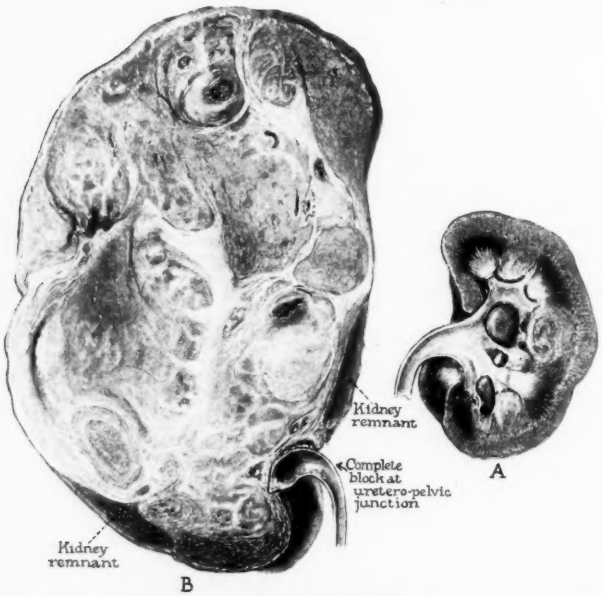


Fig. 3. Case 2. A, Normal kidney. B, Tumor removed at operation. Only a small remnant of kidney tissue remains at the lower pole. There is complete block at the ureteropelvic junction.

abundant, surrounding the clumps of epithelial cells, than in them. In places the transverse striations of the muscle fibers were so compact that the fiber resembled a coil spring. Elsewhere the striated muscle fibers had a heterogeneous arrangement.

The sections of the nodular surfaces made by cutting consisted of compact epithelial cells with deep chromatin stain and were surrounded by a loose network of cells with finely granular, almost spherical, nuclei which stained faintly. Red blood cells were present out in the tissue and in the delicate capillaries.

Sections of the tumor removed 4 months after surgical exploration of the tumor with biopsy, were essentially similar.

CASE 2. H. D., male, white, aged 2 years, referred by Dr. Reichert, was admitted to the Children's Memorial Hospital on the service of Dr. Joseph Brennemann, September 5, 1928. The mother had noticed the presence of a large mass in the abdomen 1 month prior to admission. The mass had definitely increased in size. It was the mother's opinion that the mass fluctuated as to size, at times being larger and at other times, smaller; but her general impression was that the mass had become definitely larger. There were no subjective symptoms except that the child appeared to be weak and poorly nourished.

Physical examination disclosed a poorly nourished, anæmic, flabby child, active, and mentally alert. Head, neck, and lungs were negative. A systolic murmur was heard at the base. A large mass in the left upper abdominal quadrant was more easily palpable in the flanks than anteriorly. The mass was smooth, firm, and irregular in outline. Temperature on admission was 102 degrees. During the child's stay in the hospital it varied from 102 to 103.5 degrees. Blood examination showed red blood cells, 2,000,000; white blood cells, 9,000; hæmoglobin, 40 per cent; polymorphonuclear neutrophiles, 51 per cent; lymphocytes, 44 per cent; eosinophiles, 3 per cent; transitionals, 2 per cent. Blood chemistry examination revealed urea, 60; urea nitrogen, 28; uric acid, 5.5; creatinin, 1.6; non-protein nitrogen, 44; cholesterol, 250. Urinalysis showed albumin, faint trace; pus, 0; blood, 0; casts, 0. Wassermann test was negative. Father's and mother's Wassermann tests were negative. Roentgen-ray examination of the chest was negative.

Cystoscopic examination showed the bladder to be normal. The right ureter was catheterized. Examination of the urine obtained from the right kidney was negative. The left ureter was not catheterized. A right pyelogram showed normal kidney.

Pre-operative diagnosis: tumor of left kidney, probably malignant. Operation advised but refused.

On October 16, 1928, patient again entered the hospital. One week before this admission there had been bright red blood (?) in the urine.

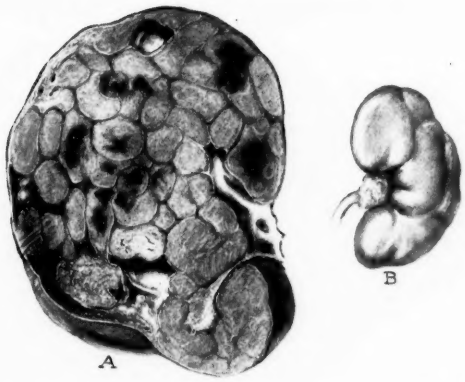


Fig. 4. Case 6. A, Note the irregular lobulations and areas of necrosis; B, and the size of tumor compared with the normal opposite kidney.

Fig. 5. Case 8. Shows areas of necrosis in the center of the tumor, which is surrounded by a capsule. The tumor has displaced over one-half of the kidney. Note the sharp line of demarcation between the kidney and the tumor.

*Operation.* (H. L. K.) October 16, 1928 (ether anæsthesia). The usual oblique kidney incision was made. An exceedingly large tumor of the left kidney was found, the whole mass being firmly bound down by adhesions. Because of its enormous size and difficulty in isolating this mass it was decided not to do a nephrectomy. A small piece was removed for histological study.

*Description of surgical specimen.* There were found diffuse epithelial cell nests; loose stroma; solitary new tubules, both inside and outside of cell nests; focal compression necrosis with suppuration; coarse striated muscle fibers in bundles.

Histological diagnosis: embryonal adenomyosarcoma of the kidney.

The postoperative course was uneventful. It was advised that the patient be given deep X-ray therapy. The child was removed to the Presbyterian Hospital where 15 such treatments were given by Dr. C. B. Rose. After the second deep X-ray treatment there was a remarkable reduction in the size of the tumor, it apparently decreasing to one-half its original size. After this diminution in size, further treatment had no effect on the tumor. Examination of the patient about one month after the institution of the X-ray treatment revealed in the abdomen multiple masses, which increased rapidly in size. Coincident with this sudden swelling of the abdominal masses a large amount of sugar was found in the patient's urine.

On December 23, 1928, the patient entered the hospital for the third time. Physical examination at this time revealed the following: The patient had an old and emaciated appearance. The arms, thighs, and legs were extremely thin, the ribs were prominent. The superficial veins of the upper abdomen and chest were very prominent. On the right side, the veins were distended to the umbilicus. In the midline was felt a swelling apart from the rest of the general abdominal distention. The left half of the abdomen was tense and a large nodular mass was felt on the right side of the abdomen. It was hard and extended down to the umbilicus. The impression conveyed was that it was due to a much enlarged liver, the result of metastases. A metastatic nodule was noted in the right testicle. Urinalysis revealed a cloudy urine; reaction, acid; albumin +++; sediment, loaded with bacteria; pus, 0; blood, 0; casts, 0. Blood examination showed red blood cells, 2,320,000; white blood cells, 11,600; hæmoglobin, 45 per cent.

The patient died December 26, 1928, and autopsy was done 4 hours after death.

Anatomic diagnosis: primary embryonal adenomyosarcoma of the left kidney (Wilms tumor); dilatation of the pelvis of the left kidney; compression atrophy of the left kidney; multiple metastases to the liver and mesenteric lymph nodes; fibrous peri-splenitis; compression atrophy of the adrenal glands; implantation tumor with obstruction of the left ureter; compression dilatation of the left pampiniform plexus; compression atrophy of the liver; cholesterol deposits of the liver; malnutrition; ascites.

The essential autopsy findings were: a markedly emaciated white boy, 2½ years old, by actual weight 12⅓ kilograms, and 97 centimeters tall; a symmetrical tumor present in the left kidney weighing 1,110 grams (see Fig. 3), which had arisen within the kidney and by its growth had destroyed the kidney except for a portion of the upper pole; huge metastases into the liver, altogether weighing 2,600 grams, which compressed the liver by its rapid growth and so distorted the shape of the liver that the falciform ligament lay to the left of the midline of the abdomen and the gall bladder in the left upper quadrant of the abdomen.

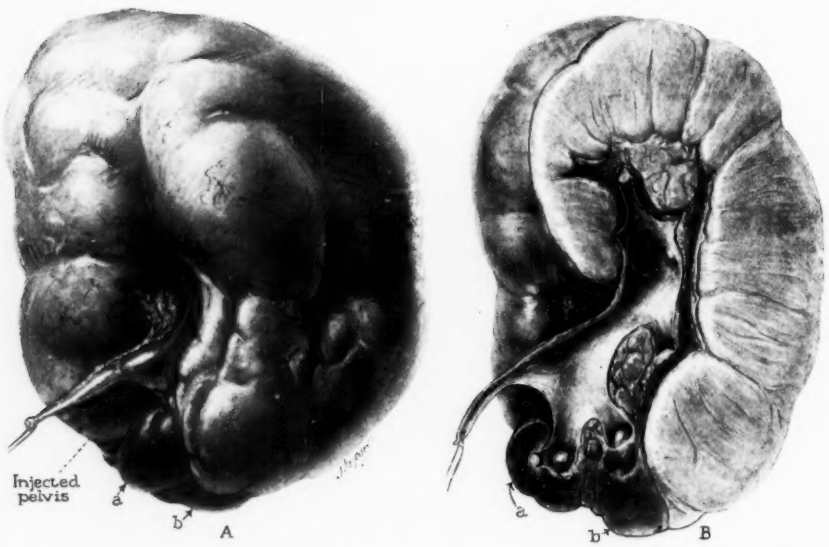


Fig. 6. Case 10. A, Specimen removed at operation showing general rounded outline of the tumor with irregular surfaces. Pelvis has been distended with salt solution, is about normal in size. B, Specimen open. *a*, Shows a small remnant of kidney tissue. *b*, Area of necrosis. There has not been much encroachment upon the kidney pelvis by the tumor.

Histological examination of the tumor of the left kidney showed loose stroma, epithelial cell nests, some of which contained tubules and others which were epithelial cell nests without tubules; striated muscle fibers in bundles; extensive compression necrosis; left ureter implantation tumor with necrosis; huge metastasis to the liver (Fig. 16), which contained epithelial cell nests and tubules; and compression atrophy of the left kidney.

Case 3. B. R., male, white, aged 5 years, was admitted to the Children's Memorial Hospital on the service of Dr. Sigurd Kraft, August 19, 1927, with the following complaint: The presence of a large mass in the abdomen. Patient had been irritable for the past 21 months. Three weeks before admission the mother had noticed the presence of a swelling in the abdomen, which apparently caused no upsets. He had not lost weight. Urinary symptoms were absent. During the past months he had had attacks of nausea and vomiting. Physical examination disclosed a thin, undernourished child, not acutely ill and not in distress. The tonsils were slightly enlarged and reddened. The heart and lungs were negative. A large mass was present in the upper left quadrant of the abdomen and extended 1½ inches to the right of the midline and well down into the lower left quadrant. The mass was smooth, rather firm in consistency, not tender, and moved with respiration. The edges of the mass were well defined. Upon palpation it would seem that the tumor sprang from the left kidney. The external genitalia were negative. Temperature was 99 degrees. Blood examination showed red blood cells, 3,890,000; white blood cells, 9,600; hæmoglobin, 70 per cent; polymorphonuclear neutrophiles, 75 per cent; lymphocytes, 24 per cent; transitionals, 1 per cent. Von Pirquet test was negative. Urinalysis revealed reaction, acid; albumin, 0; sugar, 0; sediment, few hyalin and granular casts; occasional red blood cells; occasional white blood cells. Roentgen-ray examination of the chest was negative; of the abdomen revealed a circular opaque shadow occupying the left upper quadrant and extending over to the right side beyond the midline.

Pre-operative diagnosis: malignant tumor of the left kidney.

*Operation.* (Dr. E. M. M.) August 22, 1927 (ether anæsthesia). The usual kidney incision was made. An exceedingly friable tumor was removed, and the vessels were ligated. The wound was closed with drainage.

Histological diagnosis: sarcoma—multiple cell type—of left kidney.

The postoperative course was uneventful. The patient received six deep X-ray treatments and was discharged from the hospital on October 4, 1927. Examination before the child left the hospital revealed the presence of a large recurring tumor. Patient died April 13, 1928.

*Description of surgical specimen.* The kidney and multiple surgically excised portions of tumor tissue

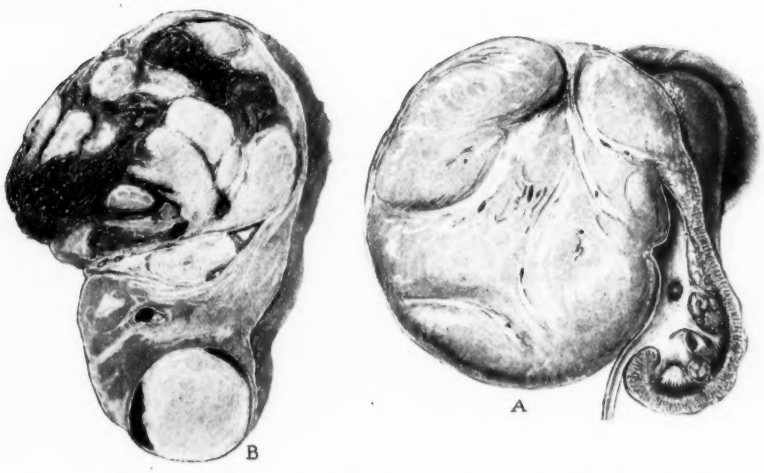


Fig. 7. Case 12. A, Specimen removed at first operation. Sharp line of demarcation of tumor. B, Specimen of remaining kidney removed at autopsy.

together weighed 450 grams. The surgically excised portions varied from 2 to 30 grams in weight; they were soft, friable, occasionally smooth, compressible, and dark brown.

The tumor arising from the back portion of the lower pole was sharply defined from the attached kidney.

Microscopic examination showed between the tumor and the kidney itself fibrous tissue layer. The kidney itself was normal except for compression where it was adjacent to the tumor and here the kidney intertubular tissue was increased and fibrous. The tubules were irregular in size and shape and had large nuclei which because of the coarse granules stained deep with hematoxylin. Some of the kidney tubules contained leucocytes, both polymorphonuclears and lymphocytes, but in the fibrous band between the kidney and tumor itself there was an infiltration also of polymorphonuclear leucocytes and lymphocytes. Deeper into the tumor was a loose stroma network (Fig. 15) containing multiple new tubules which were usually small and round, but some of them had folded walls to produce a papillary structure. Epithelial cells were scattered throughout but there were no real epithelial cell nests here. Elsewhere in the tumor the stroma was infiltrated with large, pale stained epithelial cells with nuclei which contained fine granules. These cells were evenly scattered throughout the stroma and although they did not occur in true epithelial cell nests, they were present in compact clumps. Throughout the tumor there were strands of smooth muscle but no definite striated muscle was present.

Case 4. W. W., male, white, aged 5 months, was admitted to the Children's Memorial Hospital on the service of Dr. Joseph Brennemann, August 24, 1923. At this time the mother stated that 1 month before admission to the hospital she had noticed a swelling on the left side of the abdomen just below the costal margin. When first discovered the tumor was about 3 or 4 inches in diameter, but it rapidly grew larger, so that now it filled the entire left side of the abdomen, causing a marked bulging. The mother had noticed no loss in weight, no constipation, and no urinary symptoms. Physical examination disclosed a well-nourished white infant, playful and smiling. The heart and lungs were negative. The abdomen showed a rounded, bulging tumor mass filling the entire left half and bulging into the flanks. The skin was tightly stretched over the mass and was shiny. The mass was firm in consistency, a little more prominent in front to the left of the navel for about 2 inches. On palpation, the mass could be outlined along the midline midway down in the left lower quadrant but the upper limits were lost under the arch of the ribs. The circumference of the abdomen at this point was 18.5 inches. The testicles were not in the scrotum. The temperature was 99.2 degrees on admission. Blood examination showed red blood cells, 3,100,000; white blood cells, 26,200; hæmoglobin, 55 per cent; polymorphonuclear neutrophiles, 46 per cent; small lymphocytes, 44 per cent; large lymphocytes, 4 per cent; large mononuclears, 1 per cent; transitionals, 2 per cent; eosinophiles, 3 per cent. Urinalysis showed clear urine; reaction, acid; albumin, 0; sugar, 0; blood, 0. The von Pirquet was negative. Roentgen-ray examination of the abdomen showed all shadows obscured by a large opaque shadow occupying the entire left abdomen.

*Operation.* (Dr. A. F. M.) August 30, 1923 (ether anæsthesia). Exploratory operation only was done. The child died, August 31, 1923.

Autopsy was done 3 hours after death. The anatomic diagnosis was bilateral embryonal adenomyosarcoma (huge of the left kidney and slight of the right kidney); abdominal viscera displaced to the right; pressure atrophy and partial hydronephrosis of the left kidney; recent surgical abdominal exploratory operation wound; generalized anæmia; hyperplasia of the thymus, spleen, and lymphoid tissue of the lining of the bowel; hypostatic hyperæmia and œdema of the lungs; slight hypostatic bronchopneumonia; cloudy swelling of the liver and right kidney; fatty changes of the liver and right kidney; dry and crusted lips; unequal pupils; undescended testicles; partial congenital sinus of the right ureter; accessory spleen.

The essential autopsy findings were: the patient was a 5 months old boy; weight 12.5 pounds, and height 62.5 centimeters. A huge, solid tumor was present in the left kidney which weighed 545 grams and displaced the abdominal viscera to the right. A second tumor of the lower pole of the right kidney was pale gray, and sharply defined in marked contrast to the adjacent compressed kidney. There was no evidence of metastasis anywhere in the body.

Microscopic examination of the kidney tumors revealed dense epithelial cell nests; rather dense epithelial stroma, tubules both in epithelial cell nests and solitary in the loose stroma. The tubules were sharply defined and were very similar to those of a normal kidney. Compression atrophy of the kidney, center liquefaction necrosis, and dense masses of sharply defined striated and non-striated muscle fibers were noticeable.

Case 5. R. F., female, white, aged 5 years, was admitted to the Children's Memorial Hospital on the service of Dr. S. J. Walker, December 22, 1914, with the history that 4 months before admission to the hospital, that is, when the child was about 4½ years old, she ran along the top of a wall and fell to the ground striking her abdomen against the wall. After this the mother noticed a small, hard lump a little larger than a hen's egg in the abdomen. Two days after the injury the child vomited a good deal. Subsequently a large hard swelling developed in the abdomen which increased rapidly in size. The child was constipated and bowel movements were painful. There have been no urinary symptoms; no history of blood in the urine or fæces. During the 2 years before admission, the child had lost some weight. There was pain in the abdomen which was most marked in the left side, and the pain was worse at night. Physical examination disclosed a rather poorly nourished but well developed child, able to walk about the ward with comfort. The skin had a sallow, tan color. The teeth were in poor condition. The heart was normal except for a systolic murmur. The lungs were negative. In the abdomen was a marked enlargement due to a tumor mass. Veins over the entire abdomen were large. The suprapubic region and the lower right iliac region were the only places free from this mass. In the right upper quadrant there was felt an oval mass about the size of a fetal head, approximately 10 by 10 centimeters. This mass had a cystic feel and was surrounded by an area of comparative tympany. The mass moved partly with respiration. There were a few enlarged anteroposterior cervical and submaxillary lymph glands, as well as a few palpable inguinal glands. The veins of the extremities were prominent. Temperature on admission was 101 degrees. Blood examination revealed red blood cells, 4,160,000; white blood cells, 8,200; hæmoglobin, 80 per cent; stained blood smears were negative. The blood Wassermann test was negative. Urinalysis revealed reaction, acid; albumin, +; sugar, 0; sediment, few white blood cells; and few hyalin casts. The phthalein test showed 30 per cent secretion in 2 hours. Cystoscopic examination of the bladder was negative. The ureteral catheter met an obstruction on the left side. Three catheters were passed into the ureter for about ¾ inch, beyond which point catheters could not be advanced. A pyelogram was attempted through this catheter but the fluid failed to reach the kidney.

Pre-operative diagnosis: malignant tumor of the kidney.

*Operation.* (Dr. B.) January 7, 1915 (general anæsthesia). A right nephrectomy was done. The child died, January 28, 1915.

The surgical specimen consisted of the kidney and its adherent tumor which together weighed 265 grams. The kidney was essentially of uniform, globoid shape with lobules elevating the surface capsule. The tumor arose centrally in the kidney and by its growth pushed the normal kidney outward. The kidney tissue which remained was sharply defined, definitely separated from the tumor, and the kidney was so compressed in places that it was only 3 to 4 millimeters thick. The tumor itself consisted of lobules 5 to 20 millimeters in diameter which were gray to pink, firm, and of even consistency throughout. The lobules were separated from each other by fibrous bands, and in several of these lobules there were dark red to black, soft, friable portions 1 to 3 centimeters in general diameter.

Microscopic examination revealed dense epithelial cell nests with large nuclei which were coarsely granular; the epithelial cell nests had isolated tubules in their centers and elsewhere the central walls of the epithelial cell nests were clumped or agglutinated together as in the formation of new tubules. Fibrous bands ramified throughout the tissue. Single strands of striated muscle fibers were present throughout the diffuse loose stroma.

Case 6. W. A., male, white, aged 3 months, admitted to the Children's Memorial Hospital on the service of Drs. Buford and Walker, July 1, 1915. The present illness began 6 days ago with anorexia, vomiting, crying, fever, and constipation. He had always slept well until the night before admission to the hospital. Apparently he was in a good deal of

pain most of the time. No convulsions and no urinary symptoms were revealed. He had vomited every day since the onset of the illness up to and including the day of admission to the hospital. Physical examination revealed a rather poorly nourished child, who cried a good deal. The entire surface of the body was covered with a fine petechial rash. The heart and lungs were negative. Very prominent superficial veins were noticeable on the abdomen which was rigid. A large tumor mass was palpated on the right side. The mass was round in outline, hard in consistency, and well defined, extending from beneath the costal arch into the inguinal region and into the midline as far as the umbilicus.

Rectal examination revealed the lower pole of the tumor mass extending to the right side of the pelvis. During the time in the hospital, the highest temperature was 99.2 degrees, and this occurred only once; twice the temperature was 99 degrees. Blood examination revealed white blood cells, 28,650; polymorphonuclear neutrophiles, 46 per cent; small lymphocytes, 54 per cent. The blood Wassermann was negative as were those of the father and mother. The Von Pirquet was negative. Urinalysis disclosed turbid urine; reaction, acid; albumin, +; sugar, 0; sediment, 0. The phthalein test showed only the slightest trace of dye at the end of a 2 hour period of collection. Roentgen-ray examination of the abdomen after bismuth feeding revealed the stomach displaced to the left and most of the intestines in the left side of the abdomen; the liver and tumor occupying the whole right side as evidenced by a shadow that extended from the fifth rib into the groin.

The child died, July 13, 1915, without operation.

*Autopsy.* (Incision of the abdomen only was allowed.) The body was that of a moderately emaciated white boy 18 inches tall. There was a marked protuberance of the upper right quadrant of the abdomen. Here there was a large, hard, irregular mass which extended from the costal arch above to the right anterior iliac spine and to a little left of the midline of the abdomen. The mass was lobulated and slightly movable. When the abdomen in the region of the tumor was opened there was found a lobulated mass the size of the patient's doubled fists, occupying the right kidney region. Across the lower median pole there was a loop of small bowel, but this was not adherent to the tumor mass. The fibrous capsule of the mass was opened and the tumor was easily shelled out. The right adrenal gland was in normal position and was not enlarged. The right ureter was twice as large as the left, but its pelvis was not distended. A fine probe was passed from the bladder in the right ureter, and an obstruction was met a short distance from the bladder. The left ureter was patent. The left kidney had a dime-sized subcapsular hæmorrhage. The surfaces made by section were hyperæmic and were without pathological change. The left adrenal was like the right in all essentials. The lining of the urinary bladder was enlarged. On section of the tumor mass there were found many soft lobulations from which a pink fluid was expressed. The arrangement of these friable masses in general corresponded to the markings of a kidney, but only slightly so. Beneath the capsule there was a thin structure surrounding the entire mass which resembled the cortex somewhat. There were a few cavities throughout the mass which contained pink-yellow semi-fluid. The liver, spleen, and gastro-intestinal tract were unchanged.

Anatomic diagnosis: sarcoma of the right kidney; occlusion of the right ureter.

The preserved right kidney mass weighed 295 grams; the left kidney, 13 grams (Fig. 4). The left kidney was normal in all essentials. The right kidney mass measured 11 by 7 by 8 centimeters. It was everywhere encapsulated; its surface was irregular due to nodulations 1 to 3 centimeters in general diameter as measured on the surface. On 6 surfaces made by cutting, at least $^{9}/_{10}$ of the entire mass was of tumor tissue. These surfaces were uniformly smooth, glistening, and uniformly firm. These surfaces consisted of single nodules 5 by 8 millimeters in general diameter to conglomerate masses 3 to 3.5 centimeters in diameter. These conglomerate masses were largely of the upper pole. An irregular mass of the lower pole about 3 centimeters across was dark brown, glistening, lobulated and had a suggestion of striations of the cortex and pyramidal portion. It cut with the consistency of the normal kidney. It was the only structure which grossly resembled what was left of this kidney tissue. The tissue between the light brown to gray fibrous-like tumor nodulations, was soft, friable, dark brown, and brown-black stippling as in old blood exudation. On close inspection this internodulation tissue resembled compressed kidney tissue. All sections made by cutting were similar. The pelvis of this right kidney and the tumor mass were not a single sac, but rather consisted of irregularly dilated sacculations, some of which were 1 centimeter in circumference. These sacculations were normally thin walled, had glistening linings, and these were irregularly fused to converge at the ureter, which was 3 millimeters in circumference and grossly resembled the left ureter in all essentials. In the lower pole, between the kidney tissue and the tumor tissue, three sacculations of this pelvis measured 3 to 10 millimeters long and 2 to 5 wide. These were the only places where the pelvis was distended. (Drawings were made to show the gross appearance of the right kidney tumor mass in relative size to the normal left kidney.)

Microscopic examination showed large clumps of loosely packed epithelial cells in a fibrous reticulum. New tubules were abundantly present in the peripheries of the epithelial cell masses. The tubules were of irregular shape and in general were larger than a normal tubule; they were sharply defined. Tubules were present both within the cell nests and in the loose stroma in such huge number that 36

were counted in a single low power field. Elsewhere there were masses of large epithelial cells clumped together in their central portions as in the formation of new tubules. Single strands of striated muscle fibers were present, but thick bundles of nonstriated fibers were abundant. There was diffuse anæmic compression necrosis with focal suppuration.

CASE 7. F. O., male, white, aged 6½ years, was admitted to the Children's Memorial Hospital on the service of Dr. Gustav Kaufmann, March 10, 1919. Two weeks before admission the child suddenly complained of severe pain in the right side of the abdomen following a bowel movement. He was nauseated and vomited. Temperature rose to 103 degrees. The temperature, nausea, and vomiting persisted for several days. Physical examination disclosed a decidedly anæmic child who was apparently in great pain. The pupils reacted to light. The teeth were in poor condition. The tongue was very red; the tonsils, enlarged and reddened. The neck showed moderate lymphadenopathy. The chest had a marked rachitic rosary. The heart disclosed a roughened first sound at the apex which was transmitted to the axilla and toward the base. The lungs were negative. A bulging tumor mass was noticeable in the right upper quadrant. It extended just a little beyond the midline and about one-third of the distance between the costal arch and the crest of the ilium and did not move with respiration. A peculiar crepitant sensation was elicited upon palpation. The records stated that this was like a subcutaneous emphysema. Temperature on admission was 103 degrees and came down to normal in 72 hours. Following the operation, temperature rose to 104.5 degrees. Blood examination revealed red blood cells, 2,650,000; white blood cells, 22,700; polymorphonuclear neutrophiles, 85 per cent; small lymphocytes, 4 per cent; large lymphocytes, 4 per cent; transitionals, 3 per cent; myelocytes, 4 per cent. Urinalysis showed reaction, acid; albumin, +; sediment, white blood cells. Many urinalyses showed the presence of albumin but no casts. Roentgen-ray examination of the colon by air inflation showed the ascending and transverse colon above the tumor mass. The previously felt crepitation had disappeared.

*Operation.* (Dr. B.) March 13, 1919 (ether anæsthesia). Exploratory laparotomy in the midline was done. The peritoneal cavity was negative. A large retroperitoneal tumor mass was found in the right kidney area. The abdominal incision was closed and a right posterior incision made. A nephrectomy was done.

The postoperative course was complicated by diphtheria and measles. Examination by Dr. H. Helmholz, May 15, 1919, revealed the presence of a palpable mass in the right kidney region. Patient developed a bronchopneumonia on May 19, 1919. Great abdominal distention developed, May 28, 1919. Patient was taken away from the hospital, May 28, 1919, against advice. He was cyanotic; respiration was labored; the abdomen was greatly distended; and signs of fluid were noticeable in the abdominal cavity.

Death occurred 4 days after being taken home.

The surgical specimen consisted of the kidney and its attached tumor which together weighed 165 grams. The tumor arose centrally within the kidney and pushed the kidney tissue outward with compression of its opposite poles. The kidney tissue present was dark brown and sharply demarcated from the light gray-pink tumor tissue. The tumor was of uniform consistency, soft, compressible, except for soft, friable, porous places which were dark red to black.

Microscopic examination showed that the kidney was normal except for tubular degeneration. Between the kidney and tumor was a fibrous reticulum containing lymphocytes, then a dense cell mass of small epithelial cells and leucocytes. The next layer was a pale stained, necrotic mass of tissue which stained with eosinophile only except for isolated leucocytes which were blue with hematoxylin. The tumor itself consisted of dense epithelial cell nests and loose cell masses of epithelial cells with isolated tubules in the cell nests, and in places there was an agglutination of cells in the central portions of the epithelial cell nests forming tubules. Between lobules there were masses of tissue of compression anæmic necrosis, portions of which contained disintegrated leucocytes.

CASE 8. R. W., male, aged 2½ years, admitted to the Presbyterian Hospital on the service of Dr. C. G. Grulee, January 5, 1925, with the complaint of a mass in the abdomen. Six weeks ago while the child was standing up the mother noticed the presence of a swelling the size of an orange in the left upper quadrant. This mass had gradually increased in size, growing toward the midline. For the past 6 months he had had difficulty in passing urine in that it was necessary for him to strain considerably at each urination, but pain was absent. He voided several times a day in large amounts. No blood was found in the urine at any time. He had slept well, and had lost no weight. Physical examination by Dr. C. G. Grulee revealed a well developed and well nourished child. The head and neck were negative except for slightly enlarged tonsils. A few enlarged, shotty glands were felt in the posterior triangles of the neck. There was slight dullness in the left lower lobe of the lungs posteriorly and the excursion of the diaphragm was limited. A mass was felt in the left upper quadrant extending well below the umbilicus below and 2½ inches beyond the midline to the right. The tumor was firm and smooth except for an apparent lobulation above the midline. The external genitalia were negative as were the extremities. Blood examination showed: red blood cells, 4,280,000; white blood cells, 6,600; hæmoglobin, 85 per cent. Urinalysis showed reaction, acid; albumin, 0; sugar, 0; blood, 0; bile, 0; sediment, 0. Cystoscopic examination showed the bladder to be normal. The ureters were normal and could be catheterized without difficulty or obstruction.

Urines from the right and left kidneys and bladder were sterile and free of pus. Indigocarmine test showed a concentrated discharge of blue urine from the right side in 10 minutes and a very dilute, pale blue urine from the left side in 15 minutes. Roentgen-ray examination disclosed a dense shadow involving the greater part of the left side of the abdomen. Pyelogram of left side was normal. Pre-operative diagnosis: in spite of the fact that the left pyelogram was normal a diagnosis of malignant tumor of the left kidney was made and operation was advised.

*Operation.* (H. L. K.) January 12, 1925 (ethylene anæsthesia). Through the usual oblique kidney incision a left nephrectomy was done.

Recovery was uneventful and patient was discharged, January 30, 1925.

The surgical specimen consisted of the entire kidney mass which weighed 294 grams (Fig. 5). In general it was pear-shaped, the stem portion consisting of grossly normal kidney, the base of which flattened out broadly into the huge tumor mass, from which the kidney was separated by fibrous bands. Approximately ⅓ to ½ of this original kidney was present. Its cortex was easily 2 to 3 millimeters wide. Its striations were normally present in relation to the medullary portion. The entire mass was normally encapsulated. This capsule readily stripped off from the kidney proper, but where the kidney was flattened out to blend into the broad tumor mass, the capsule was rather firmly adherent and took fine shreds of tumor tissue with it when separation of the capsule and the tumor was attempted. After removal of the capsule, however, the general surface was found to be essentially smooth and light gray to light brown, in sharp contrast to the adjacent dark brown kidney tissue.

On surfaces made by cutting, about $^4/_5$ of the tumor mass was found to be rather firm and in places friable. It was light gray to brown and of essentially equal consistency, centrally as peripherally. The remaining $^1/_5$, which was of the lower pole, was soft and mushy; it was lighter gray and putty-like in consistency. Here pressure necrosis was definite.

Microscopic examination showed dense epithelial cell nests with large, coarsely granular nuclei which were vacuolated; the nests contained huge, well-formed tubules, some of which were in the process of formation. The nests were separated by fibrous tissue strands and in some of these nests there were masses of disintegrated leucocytes. Tubules were abundant. There were masses of pale-stained, epithelial, cellular stroma of compression necrosis; many non-striated muscle fibers; solitary single strands of striated muscle fibers; dense fibrous stroma in which were scattered large epithelial cells with coarsely granular vacuolated nuclei.

Case 9. B. B., male, white, aged 19 months, admitted to the Children's Memorial Hospital on the service of Dr. Charles Schott, November 13, 1924. The present complaint was a large mass in the abdomen. As far as the father knows, the child was perfectly well until about 2 months before admission when he became very nervous, developed a poor appetite, and did not appear to be well. He also began to lean forward when urinating. He was taken to a physician who advised circumcision, and this was done. A week following the circumcision, or 4 weeks before admission to the hospital, the mother found a mass in the left side of the abdomen. No urinary symptoms. The child had had some fever off and on since the circumcision. Physical examination by Dr. C. Schott revealed a fairly well developed, rather poorly nourished child who did not appear acutely ill. The chest was moderately emaciated and presented a slight Harrison's groove and rachitic rosary. The lungs were negative. The heart was negative. The abdomen disclosed a bulging of the left flank. A very large, hard tumor mass filled the whole left flank and the whole abdomen to the left of a line about 1 centimeter to the right of the left nipple. The mass was regular except a protuberant portion about 1 inch above the umbilicus which extended from the tumor mass proper to the midline of the abdomen. It was hard and was attached to the main tumor, about 2 centimeters across. It was possible to palpate between the tumor and the costal margin from the anterior axillary line to the right. The mass was not tender, and the skin was not discolored. The liver and spleen could not be felt. The external genitalia were negative.

A second examination by Drs. Schott and Brennemann verified these findings. Rectal examination showed a tumor mass palpable and extending down into the pelvis. The lower pole was smooth, rounded, and not tender. Colon inflation revealed the colon passing over the tumor mass. Temperature on admission was 99 degrees and never went higher. Blood examination showed white blood cells, 6,200; hæmoglobin, 75 per cent. The nasal and throat cultures were negative. Fluoroscopic examination with barium verified the previous colon examination. Roentgen-ray examination showed the chest to be negative for evidence of metastasis. The abdomen, following barium enema, showed a filling defect in the descending colon which was accounted for by intra-abdominal pressure.

Pre-operative diagnosis: sarcoma of the left kidney. Operation was advised.

*Operation.* (Dr. E. M. M.) November 21, 1924 (ether anæsthesia). Nephrectomy was carried out. Patient died on the table.

*Autopsy.* (Autopsy examination was made through the surgical wound only.) The anatomic diagnosis was mixed cell tumor of the left kidney with abdominal content displaced to the right; acute anæmia; emaciation. The organs were all found to be grossly normal and nowhere were there any metastases present either in the lungs or abdominal cavity.

The right kidney was normal in every respect and weighed 68 grams. The surgically removed left kidney and its adherent tumor together weighed 675

grams. The tumor arose centrally and compressed the kidney outward so that the kidney itself was sharply defined from the tumor mass, from which it was separated by fibrous bands and was essentially a nob of kidney tissue, the main portion of which measured about 2 by 3 by 1.5 centimeters and thinned out to newspaper thickness at the tumor margin. The tumor itself was firm to hard, of uniform consistency throughout. When cut across in several places it was found to be lobulated in places 2 to 3 centimeters in diameter and the lobules were gray to pink and some contained dark red to black, soft, friable spots.

Microscopic examination revealed a loose stroma hugely infiltrated with epithelial cells in an even arrangement, but in portions of the sections larger epithelial cells were arranged in nests containing indistinct, partially formed, new tubules. Throughout the epithelial stroma there were solitary fibers of striated muscle. In multiple places there were compression necrosis and masses of disintegrated leucocytes and débris.

CASE 10. L. J. W., female, white, aged 13 months, was admitted to the Children's Memorial Hospital on the service of Dr. Joseph Brennemann, October 8, 1928. The parents stated that the baby had always had a very large, prominent abdomen and that this had been noticed since she was about 1 month old. They did not attach importance to this enlargement until the baby was 13 months old when they took her to a doctor because it was their impression that the abdomen was growing larger than the rest of the body. The doctor made light of the mother's story and expressed the opinion that the baby would outgrow the condition. Another doctor was consulted and a diagnosis of tumor of the kidney or enlarged spleen was made. On several occasions the mother noted blood in the bowel movement. There were no urinary symptoms. Physical examination by Dr. J. Brennemann disclosed a well nourished child with a strikingly large abdomen. The tonsils were enlarged. On the left side of the abdomen was a large mass which was firm, movable, and not nodular, and occupied practically the whole of the left side of the abdomen, extending well back into the flanks. There was a small tubular mass just to the left of the navel above the other mass. Blood examination revealed red blood cells, 6,330,000; white blood cells, 14,840; hæmoglobin, 60 per cent; polymorphonuclear neutrophiles, 30 per cent; lymphocytes, 66 per cent; eosinophiles, 4 per cent. Urinalysis showed reaction, acid; albumin, +; sugar, 0; sediment, much amorphous material. Fluoroscopic examination, with barium meal, showed the intestines anterior to the mass and very close to the abdominal wall. Roentgen-ray examination showed that no evidence of metastasis was present in the chest. Cystoscopic examination revealed a normal bladder. Both ureters were catheterized without difficulty or obstruction. The urine from the right kidney was normal. No urine was obtained from the left side. Pyelograms were made and the right was normal. On the left side, the bromide solution met an obstruction at the ureteropelvic junction, hence no pyelogram was obtained. The filling defect was due to a tumor.

Pre-operative diagnosis: malignant tumor of the left kidney.

*Operation.* (H. L. K.) October 18, 1928 (ether anæsthesia). The usual oblique kidney incision was made, and the tumor was delivered through the wound, the ureter being clamped and divided. The renal pedicle was clamped and ligated. The usual wound repair (Fig. 6) was carried out. The post-operative course was uneventful. Since leaving the hospital the patient has had two courses of deep X-ray treatment. Examination showed no sign of recurrence. A recent examination, November 12, 1929, showed no sign of recurrence and the patient is perfectly well 1½ years after nephrectomy.

The surgical specimen consisted of the kidney and its adherent tumor which together weighed 785 grams. Only a small portion of the kidney had not been obliterated by compression. The tumor itself was of uniform, firm consistency; in general it was semi-spherical, about the size of a grapefruit. When cut across it was found to be firm to hard, of even consistency throughout. It was easily shredded and generally gray tinged with pink.

Microscopic examination disclosed marked compression atrophy with extensive tubular degeneration; diffuse epithelial cell stroma with clumps of epithelial cells of nest-like structure. The nuclei of the epithelial cell nests stained deeply, but the epithelial cells in the stroma had large nuclei which were finely granular and contained vacuoles. Elsewhere throughout the tumor tissue the epithelial nests were abundant, compact, together, and in their central portions retained many new tubules. Adjacent to isolated cell nests were striated muscle fibers usually in single strands.

CASE 11. A. G., male, aged 6 years, admitted to the Children's Memorial Hospital on the service of Dr. A. H. Montgomery, April 28, 1921. Two months before admission to the hospital the patient fell down, striking his left side against a bench. Pain was present in the side for about a fortnight and then disappeared. Pain recurred in the left side 3 days before entering the hospital, at which time a very large swelling was noted. A doctor was called and found the presence of a large, left upper quadrant tumor. He aspirated the stomach but no pus or fluid was obtained. The appetite was good. The bowels were normal; urination was normal. Physical examination disclosed a fairly well developed and well nourished child. The head, neck, nose, throat, heart, and lungs were negative. In the abdomen was a very large, firm tumor in the left upper quadrant, extending into the right half of the abdomen in the region of the umbilicus down to within 1 centimeter of the crest of the ilium on the left. The tumor was movable, had definite borders, and a notch could be felt along the superior surface. No tenderness was elicited on palpation. Blood exami-

nation showed red blood cells, 4,200,000; white blood cells, 12,200; hæmoglobin, 80 per cent. Urinalysis disclosed reaction, acid; albumin, 0; sugar, 0; casts, 0; leucocytes, 0. Roentgen-ray examination showed a very large tumor mass extending from the region of the left kidney, beyond the midline, and down into the iliac fossa. Examination of the abdomen by H. L. K. disclosed a large, hard, irregular, movable tumor which extended beyond the umbilicus. A notch could be felt. The lower edge was smooth and hard.

Pre-operative diagnosis: sarcoma of the left kidney.

*Operation.* (Dr. A. H. Montgomery). May 19, 1921 (ether anæsthesia). Exploratory laparotomy was performed, and a section was removed for histological study. The wound was closed. Patient left the hospital on June 11, 1921, with condition unchanged, and died.

Microscopic examination of the specimen removed showed fibrous tissue stroma containing isolated epithelial cell nests in which were new tubules. Isolated tubules were also present out in the loose stroma.

CASE 12. J. B., male, white, aged 1 year, was admitted to the Presbyterian Hospital on the service of Dr. H. L. Kretschmer, July 17, 1929. The present complaint was enlargement of the abdomen and a tumor mass on the right side. Six weeks before admission to the hospital when bathing the child the mother noticed that the abdomen seemed large. Her mother-in-law felt the abdomen and noticed a very hard, nodular mass in the right hypochondrium. The mass was not painful and increased in size very slowly until 2 weeks ago, when growth was rapid, the tumor extending from the costal margin to the crest of the ilium. No urinary symptoms were present and there was no blood in the urine. Physical examination disclosed a fairly well developed and well nourished child with head, neck, heart, and lungs negative. A large tumor was found in the right upper quadrant, extending from the arch of the rib down to the crest of the ilium and 2 fingersbreadth beyond the left of the umbilicus. The mass was firm, smooth, elastic, and freely movable; the borders were easily palpable. Blood examination showed red blood cells, 4,000,000; white blood cells, 16,200; hæmoglobin, 68 per cent. Wassermann and Kahn tests were negative. Blood chemistry examination (before operation) showed urea nitrogen, 23.4; uric acid, 5.0; creatinin, 22; total nonprotein nitrogen, 41.7. Four days after operation: Urea nitrogen, 100; uric acid, 9.1; creatinin, 4.3; total nonprotein nitrogen, 126.9. Urinalysis showed reaction, acid; sugar, 0; albumin +; blood, 0; red blood cells, rare; leucocytes, rare. Roentgen-ray examination disclosed a uniform dense shadow over the right half of the abdomen. Cystoscopic examination revealed a normal bladder. Ureteral catheters were passed without difficulty or obstruction. Pyelograms were made and showed the left side normal. The right ureter was displaced to the left side of the abdomen, the malposition beyond the midline being apparently due to the large tumor. No fluid entered the right kidney pelvis. Fluoroscopic examination (barium meal) showed the right half of the colon displaced to the midline.

*Operation.* (H. L. K.) July 21, 1929 (ether anæsthesia). A right nephrectomy was done.

The right kidney after excision weighed 514 grams (Fig. 7). It was encapsulated and in general was of kidney shape. Its surface generally was smooth. On 7 transverse sections made by cutting, about half of the surfaces were light gray, and the other half dark red to brown. The light gray portions consisted of tumor nodules, the largest of which measured 32 centimeters in diameter. These nodules were of even consistency centrally and peripherally; they were firm to hard and in sharp contrast to the adjacent light brown compressed kidney tissue remnants. This kidney tissue had a suggestion of cortex with striations and a few definite pyramids. The nodules were conglomerate but each nodule was separated from its neighbor by a firm, fibrous tissue band. In the lower pole where the mass was broadest, adjacent to the light gray nodules, there was dark red to brown, soft, friable tissue resembling compressed necrotic kidney tissue. Portions of compressed pyramids were definite, and from these places delicate, compressed bands of this kidney tissue extended out into the tumor mass between the nodules of tumor tissue which here were firm and pearl-gray.

Microscopic examination of the surgical specimen showed loose stroma; widely surrounding epithelial cell nests; new tubules, both in epithelial cell nests and in loose tissue; stroma bundle present; isolated striated muscle fibers.

Following the operation the child developed complete anuria. The left kidney was enlarged and tender. An indwelling ureteral catheter was left in place for 24 hours. A prompt flow of urine was obtained. Following the removal of the ureteral catheter the patient again developed anuria and the left kidney again increased in size. Blood chemistry examination at this time showed 133 milligrams of urea nitrogen.

*Second operation.* (H. L. K.) July 29, 1929, pyelotomy and decapsulation done. *The kidney was pale, slightly enlarged, and free of tumor.* Following the operation the urinary secretion started immediately, and 6 days later the urea nitrogen dropped from 133 milligrams to 29.1 The child made an uneventful recovery and was discharged, August 20, 1929, 22 days after the decapsulation and pyelotomy.

On September 23, 1929, 2 weeks prior to second admission the parents discovered the presence of a tumor mass in the left upper quadrant. One week prior to admission all of the urine was passed through a fistulous opening in the loin and no urine was passed through the urethra. Examination of abdomen revealed a fistulous opening in the nephrectomy scar and the presence of a mass the size of a small grapefruit in the left upper quadrant.

*Third operation.* (H. L. K.) September 24, 1929 (ether anæsthesia). An incision through the old scar was carried down through the skin and abdominal muscles. A large tumor involving the remaining kidney was found. It consisted of two or three independent masses that were irregular, exceedingly hard, and resembled in their gross appearance the tumor that was found on the opposite side. Histological examination of sections removed showed adenomyosarcoma.

The patient left the hospital, October 18, 1929, and was given 11 deep X-ray treatments. The child failed rapidly and died on December 22, 1929.

Résumé: This patient had a bilateral Wilms tumor. Interesting is the rapidity with which it developed in the remaining kidney, which had been operated upon July 29, 1929, because of anuria, though at the time there was no indication of a tumor. However, at the third operation, September 24, 1929, a large Wilms tumor involving the remaining kidney was found, its development covering only 5 weeks.

*Autopsy.* There was a huge extension of tumor tissue filling the cavity of the surgically removed kidney, with extensive infiltration into the liver and left kidney; there were multiple tumor nodule metastases to the lungs; extensive tumor infiltration of all the loose peritoneal tissues; and tumor compression of the pancreas.

The left kidney weighed 470 grams (Fig. 7), and at least $^9/_{10}$ of it was replaced by new tumor tissue which was smooth, homogeneous, gray to light brown, firm to hard; kidney tissue which was present was dark red-brown. The left kidney was definitely involved by infiltration rather than by origination of the tumor in the left kidney and subsequent compression of the kidney.

Microscopic examination of the left kidney revealed: Left diffuse compression atrophy and tubular degeneration; compression necrosis; loose stroma containing epithelial cell nests, most of which contained single new tubules or clumps of tubules; tubules both inside of nests and out in loose stroma; isolated striated muscle fibers; the loose stroma adjacent to the kidney retained tubules but no epithelial cell nests here. The epithelial cell stroma contained large, pale nuclei and in places the stroma contained only small nests and only partially developed tubules. Throughout the tumor there were strands of fibrous reticulum with clumps of lymphocytes. Elsewhere there was diffuse compression necrosis. The liver (Fig. 16) showed extensive tumor infiltration of loose epithelial stroma; epithelial cell nests and abundant sharply defined, new tubules and isolated striated muscle fibers. The lung (Fig. 17) showed that the nodules consisted essentially of loose epithelial cell stroma and small clumps of cells in a circular arrangement. The cells invaginated in folds which were apparently attempts of tubular formation.

CASE 13. G. F., male, white, aged 5 years, was admitted to the Presbyterian Hospital on the service of Dr. H. L. Kretschmer, April 28, 1924. The present complaint was a large swelling in the left side of the abdomen. The nurse stated that the child had always been well until 4 months before admission to the hospital, when he became restless, lost his appetite, and decided indications were apparent that his condition was subnormal. Shortly before Christmas (1923) he complained to the nurse that he had an ache in his side. The tumor mass was first noticed by the mother about 6 weeks ago. The mass had been growing progressively larger since that time. He had marked loss of weight and appetite. Pain and urinary symptoms were absent. Physical examination disclosed a small, pale, and anæmic child, indicating undernourishment and poor muscular development. The head and neck were negative. The chest had decidedly limited expansion. The left lung was relatively duller posteriorly than the right. There was a sharp flare of the left costal arch due to the abdominal tumor. The heart sounds were clear and rapid; some accentuation of the aortic sound. A large tumor mass occupied the entire left half of the abdomen, extending up beyond the left costal arch and downward into the left iliac fossa well below the crest of the ilium and to the right to the anterior axillary line. There was no notch. Blood examination showed red blood cells, 3,900,000; white blood cells, 22,000; hæmoglobin, 85 per cent. Urinalysis showed reaction, acid; albumin, 1+; sugar, 0; blood, 0; bile, 0; sediment, casts, 0; red blood cells, 0; and a few leucocytes. Cystoscopic examination was negative. The ureters were catheterized. No urine was obtained from the left side. The urine from the right side and from the bladder was sterile; no pus. The phthalein test showed 31 per cent of phthalein excreted from the right kidney in 50 minutes; no excretion from the left kidney. Roentgen-ray examination was negative for stone. Pyelograms were made. No fluid entered the left kidney pelvis, because of obstruction due to the tumor.

Pre-operative diagnosis: malignant tumor of the kidney.

*Operation.* (H. L. K.) April 29, 1924 (ether anæsthesia). An enormous, solid tumor mass was found; very vascular and firmly fixed, with large, dilated vessels. Several sections were removed for histological study. The wound was closed without attempting to remove the tumor mass. The child left the operating room in poor condition. It was felt that because of the large size of the tumor and its firm fixation, and also because of the poor condition of the child, a nephrectomy was out of the question.

The postoperative course was uneventful. Patient left the hospital, May 6, 1924.

Microscopic examination showed epithelial cell masses; spindle-shape cell masses containing new, sharply defined tubules; dense epithelial cell nests containing new, sharply defined tubules; diffuse fibrous tissue hyperplasia containing solitary epithelial cells with large, pale, coarsely granular

nuclei; isolated indistinct single strands of striated muscle fibers; extensive necrosis and compression atrophy with focal masses of disintegrated leucocytes.

CASE 14. F. L., male, white, aged 2 years, was admitted to the Presbyterian Hospital on the service of Dr. Arthur Dean Bevan, March 23, 1921. The present complaint was tumor of the abdomen. Two months ago the mother noticed that the child's abdomen was rather hard and large, but thought it not unusual. Three weeks prior to admission to the hospital he had a fall, bumping his right side on a sharp corner. Following this, his nurse noticed an enlargement of the right side of the abdomen. The mother was under the impression that the child lost some weight during the past 2 weeks, due to dieting. There was no history of pain or frequency or the presence of gross blood in the urine. Physical examination showed the head, neck, heart, and lungs to be negative. A very large tumor was found in the right side which was movable and had a dull note on percussion. Blood examination showed white blood cells, 8,300; hæmoglobin, 65 per cent. Urinalysis showed reaction, acid; albumin, 0; sugar, 0; blood, 0; bile, 0; sediment, casts, 0; occasional red blood cell and a few leucocytes. Fluoroscopic examination of the gastro-intestinal tract was negative. Roentgen-ray examination was negative.

Pre-operative diagnosis: tumor of the kidney.

*Operation.* (Dr. A. D. Bevan) March 25, 1921 (gas and ether anæsthesia). Right nephrectomy was done.

The postoperative course was uneventful and patient was discharged from the hospital, April 6, 1921.

Microscopic examination showed a fibroblastic stroma; loose undifferentiated cell stroma, which elsewhere was in dense clumps containing indistinct new tubules and clumps of cells in the formation of new tubules. The undifferentiated cells had huge nuclei with sparse, coarse granules in them; isolated, smooth muscle fibers and striated muscle fibers; fibrous tissue masses containing large epithelial cells.

CASE 15. G. B., male, white, aged 7 months, admitted to the Presbyterian Hospital on the service of Dr. Allen, June 24, 1917. The present complaint was a large mass in the abdomen and constipation. Two and a half weeks prior to admission to the hospital the mother noticed the presence of a mass in the abdomen. Previous to this time patient had been perfectly well. Constipation had been present for about a week. He had not lost weight or appetite; he had no urinary symptoms, but a slight afternoon temperature up to 101.2 degrees. Physical examination disclosed a well nourished and lively child with head, neck, heart, lungs, and extremities, negative. In the abdomen on the left side was a mass the size of a grapefruit, firm in consistency, smooth, and fairly movable, but not tender. The testes were not descended. Blood examination showed white blood cells, 8,500. Urinalysis showed reaction, acid; albumin, 0; sugar, 0; bile, 0; sediment, casts, 0; blood, 0; few leucocytes.

*Operation.* (Dr. A. D. Bevan) March 26, 1917 (ether anæsthesia). Left nephrectomy was done.

The postoperative course was uneventful and patient left the hospital, July 7, 1917.

Microscopic examination showed massive epithelial cell nests with a huge number of large, sharply defined, new tubules, both in the nests and out in the loose stroma; striated muscle fibers abundantly ramifying throughout the epithelial cell nests and fibroblastic stroma.

CASE 16. D. S., male, white, aged 3 years 10 months, was admitted to the Presbyterian Hospital on the service of Dr. C. G. Grulee, July 16, 1919. The present complaint was general weakness, pain on the right side, and stomachache. About 5 weeks before admission to the hospital, while walking down the street, he fell. He complained of pain in the right side and was carried home. He had been in bed most of the time since. On rare occasions he walked about the room, but seemed very tired. A few days after the fall the mother noticed the presence of blood in the urine, which had been present in varying amounts. At times the urine appeared free of gross blood. He had pain in the side almost continuously; pain in the left side occasionally. Urinary symptoms were absent. Physical examination disclosed a well nourished child who did not appear ill. The temperature was normal. The head and neck were negative. The chest, heart, and lungs were negative, except bronchial gland dullness extending to the third spine. The abdomen was very protuberant, more so on the right side than on the left. There was a hard, resistant tumor mass in the right upper quadrant that extended from the costal margin in a line 2 inches from the midline down to the level of the anterior superior iliac spine back to the spine in the lumbar region. The liver was palpable, being pushed over to the left. The spleen was not palpable. The left kidney was not palpable. The external genitalia were negative. Blood examination showed red blood cells, 4,050,000; white blood cells, 9,900; hæmoglobin, 85 per cent. Urinalysis disclosed reaction, acid; albumin, trace; sugar, 0; sediment, occasional hyaline and granular casts; blood, trace; many leucocytes. The Von Pirquet was negative. Cystoscopic examination revealed the bladder negative; the ureters normal, no obstruction; and urines from the right and left kidneys sterile and free of pus.

*Operation.* (H. L. K.) July 19, 1919 (ether anæsthesia). A right nephrectomy was done. The tumor was unusually large, was surrounded by many large blood vessels, and there was much bleeding due to the presence of these enlarged veins. The tumor was delivered with great difficulty, the pedicle isolated, clamped, and ligated, and the kidney and the tumor were removed. The patient left the table in very poor condition due to shock. Patient died that night. Permission to obtain an autopsy, unfortunately, was not granted.

The surface of the specimen removed was irregularly nodular in the lower half and fairly smooth in the upper half. The lower half seemed to be made up of many small nodules. One large nodular mass was situated on the convex border. On the surface of the upper part were seen many small nodules, distinct and isolated.

Surface made by cutting showed a very small amount of kidney tissue left, which formed a band at the outer side, varying in thickness, averaging 1 centimeter. The lower half of the tumor was hard and solid. The nodules were white in color with here and there a yellow tinge which seemed to be more marked in what appeared to be fibrous tissue. In the middle of the tumor, just under the surface, was a large yellow area, round in outline and about 3 centimeters in diameter. The color was sulphur-yellow (?). The upper half of the tumor was of a very dark color, extremely friable. Small nodules were seen in the renal parenchyma or what was left of it.

Microscopic examination showed huge compact epithelial cells in nests containing new, sharply defined tubules; both large and small similar tubules out in the fibrous stroma were abundant; elsewhere they were only few in number; central agglutination of cells in the epithelial cell masses forming new tubules; single strands of striated and non-striated muscle throughout the loose stroma; dense strands of fibrous tissue; diffuse focal compression atrophy with necrosis and masses of disintegrated leucocytes.

CASE 17. J. L., male, white, aged 16 months, was admitted to the Presbyterian Hospital on the service of Dr. A. H. Parmelee, December 14, 1927. Two weeks before admission to the hospital the parents noticed a mass in the upper left side of the abdomen. The mass was painful when handled and grew rapidly since it was first noticed. The child was restless and did not sleep well at night, and there was a slight rise in temperature. There were no urinary symptoms. Physical examination disclosed a well nourished child who did not appear acutely ill. The head, neck, heart, and lungs were negative. A large, palpable mass was noticed in the upper left quadrant which seemed to be connected with the left kidney. Upon palpation the mass was tender. The temperature was 99.2 degrees on admission. Blood examination disclosed red blood cells, 4,300,000; white blood cells, 10,050; hæmoglobin, 65 per cent. The Von Pirquet was negative. Urinalysis showed reaction, acid; albumin, 0; sugar, 0; sediment, occasional white blood cell; blood, 0; few red blood cells. Fluoroscopic examination (barium meal) showed displacement of the colon by a mass in the left upper quadrant. Roentgen-ray examination of chest was negative except that the diaphragm was slightly elevated, probably pushed upward by the tumor; of the abdomen showed the transverse and splenic flexure pushed down by mass filling almost the entire left upper quadrant.

*Operation.* (Dr. E. M. M.) December 16, 1927 (ether anæsthesia). Incision for exploratory laparotomy was made. A malignant tumor of the left kidney, the size of a large grapefruit presented between the spleen and transverse colon, extending 2½ inches to the right of the midline and as far to the left as one could feel; it was fixed posteriorly. No attempt was made to remove the tumor. A small piece of tissue was removed for histological study. Closure was made in the usual way.

The postoperative course was uneventful. Child was discharged from the hospital December 27, 1927, and died June 21, 1928.

Microscopic examination showed huge epithelial cell masses containing new tubules which were only poorly defined, many of them suggestive of tubule formation because of central clumping of cells. Epithelial cell nuclei were large, pale stained, and contained finely granular chromatin; diffuse fibrous tissue hyperplasia; isolated strands of non-striated muscle and indistinct striated muscle fibers stained with phosphotungstic acid hematoxylin.

### PATHOGENESIS

Distinct forms of mixed tumors of the kidney in children were first described in 1884, by Jacobi, although in 1872, Eberth described tumors of the kidney which contained more than one type of tissue, among which were muscle elements. Eberth believed that such tumors were the result of inclusions in the kidney of parts of the wolffian body. To Birch-Hirschfeld, however, belongs the credit of recognizing that these tumors have histological features common to neoplasms, and contain a mixture of epithelial and connective tissue elements which proliferate in a most extensive embryonal manner. Birch-Hirschfeld agreed with Eberth, that these tumors have their origin in remnants of the wolffian body. He says that the glandular tissue is primary and interprets the round cells as transition forms which may at any time differentiate into glandular structures.

In 1899, Wilms, whose name is often attached to these tumors, published a monograph which cleared up much of the confusion which existed regarding their origin. Wilms' explanation of the origin of the tumors has been generally accepted. He showed that mixed tumors of the kidney were composed of a variety of different tissues; that all the tissues developed from a cell tissue which did not show any of the known differentiating marks. Glandular elements were always present; smooth and striated muscle, cartilage,

fat, elastic, fibrous, and myxomatous tissue were nearly always present. Wilms disputed Birch-Hirschfeld's views for he said that although the wolffian body does contain nonstriated muscle fibers, it does not contain any striated muscle fibers which are so often present in these tumors. He assumed that these tumors arose from a scattered displacement of undifferentiated mesodermic germinal tissue which later gives rise, in the course of normal development, to the pronephros and wolffian body and to the myotomes. This undifferentiated cell tissue must, therefore, have the potential quality of being able to produce all the different types of tissue, even though with our present limited status of the knowledge of cells, this may appear too extraordinary to be plausible. In other words, the cell tissue must be an embryonal germinal variety that is still in the first stages of development.

The primary segment or myotome furnishes the entire striated musculature of the region of the neck. This myotome also furnishes the musculature for the trunk and extremities. Granting that the entire transversely striated musculature is derived from the myotome, it is evident also that transversely striated muscle fibers occurring separate from the normal muscle fibers, as in the renal tumors, must be traced back to misplaced portions of the myotome.

The smooth muscle fibers arise from the mesenchyme. Wilms states that the smooth muscle fibers have as little relation to the transversely striated ones, that is in their origin, as does adipose or cartilaginous tissue.

The possibility of development of bone is, of course, not always present, and in rare cases bone has also been found. As a rule the external conditions of bone growth necessary for the bone are absent.

Wilms believes that the glandular elements found in these tumors take their origin from the wolffian body. He is also of the opinion that they are not misplaced, in primary fashion, in the form of developed glands, but become differentiated gradually from the embryonal round cell tissue. This round cell tissue lying in alveoli has been misplaced from the wolffian body and from the round cell, and, in secondary fashion, the glandular formation

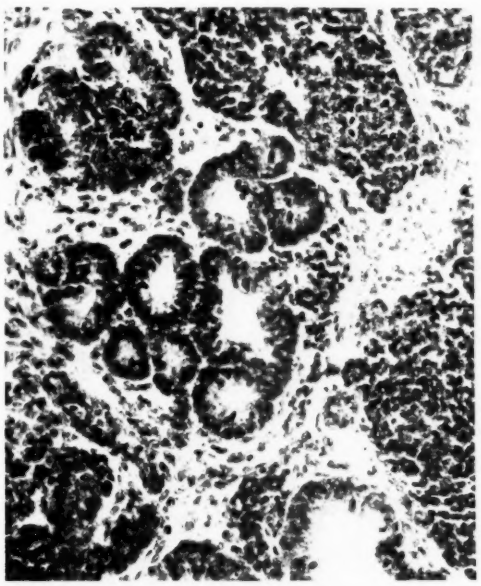

Fig. 8. The embryonic tubules which are a conspicuous feature of these tumors are sharply defined and usually present within the circumscribed masses of undifferentiated cells with dense nuclear chromatin and many mitoses. These masses of cells have been called "epithelial cell nests." (×200.)

develops. This undifferentiated embryonal tissue, when it proliferates, may thus produce the tubules that simulate those in the wolffian body; it may produce the embryonal muscle cells so often present in these growths, and if a portion of the sclerotome is carried along, cartilage also may be found. These tumors contain a mixture of tissue, any of which may predominate.

Herzog, a year later, claimed that inasmuch as tumor growth in general is regressive rather than progressive, it is not logical to assume that undifferentiated round cells later on become epithelia, first aggregated in irregular masses, then giving rise to regular tubular glands. He suggested that if the nephrotome is not cut off at the normal site, an inclusion of a portion of either the myotome, sclerotome, or both might result. Thus a matrix containing all those embryonic elements which occur in mixed renal tumors might be formed.

There has been no essential contribution to these theories since that time.

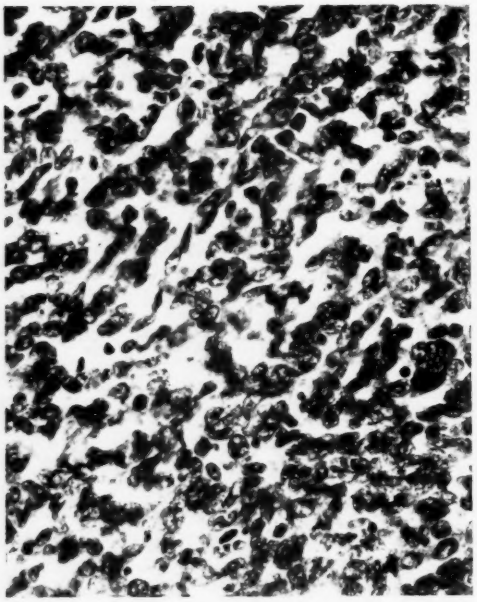

Fig. 9. Undifferentiated cells in diffuse masses without embryonic tubules are often present. These cells differ from those in the epithelial cell nests in that they are more polyhedral, have fewer mitoses, and less nuclear chromatin. (×480.)

Fig. 10. The tubules often occur in the loose stroma outside of the undifferentiated cell masses and are usually sharply defined. (×325.)

Embryonal adenosarcoma of the kidney is the most common tumor of the kidney in swine, in fact, it is the most common tumor in swine. This was first observed by Day in 1899, who, in 1907, demonstrated the similarity between these tumors in man and in swine. Young pigs usually are affected. The growth begins in one pole of the kidney, and destroys the kidney by pressure atrophy. Both kidneys are frequently affected, but metastases rarely occur. In one instance a tumor weighing 60 pounds was studied by Day.

The tumors in swine differ from those in the human (Fig. 18) in that the tubules are more abundant, more sharply defined, and many of them are folded into a papilla-like structure. Smooth muscle is abundantly present, but striated muscle has not been found. Bone and cartilage are usually present in the swine tumors but seldom in the human. These tumors have never been described in cattle or sheep.

## GROSS PATHOLOGY

Embryonal tumors of the kidney are the most common primary neoplasms which occur in children. The tumors, which are occasionally bilateral, have been described as of such size at birth as to cause dystocia. The largest of our tumors weighs 1,530 grams, the smallest, 235 grams, and the average weight of all of our tumors is 762 grams. The tumors are predominately unilateral; only 2 of the 17 are bilateral. They are encapsulated, retroperitoneal, and arise within the kidney capsule. The involved kidney usually occupies the entire side of the abdomen and displaces viscera in direct proportion to the size of the tumor. They are globular to oval shape, solid, opaque, and variously subdivided into lobules. Somewhere on the surface a nodule of kidney tissue usually remains. This kidney tissue is normal in all essentials except where it is adjacent to the tumor, where it is compressed and thins out to cover the neoplasm nearby usually for several centimeters, so that at its peripheries it may be only a millimeter thick.

Fig. 11. Cross striated muscle fibers when present usually occur in clumps throughout the stroma and occasionally in definite bundles. (×750.)

Fig. 12. Higher magnification of same section as shown in Figure 4.

These tumors arise within the kidney itself, they may occur in any portion of it, and compress the kidney so that it undergoes pressure atrophy. The kidney takes no part in the tumor formation, so that a layer of fibrous tissue free of renal structures separates the tumor from what remains of the compression atrophied kidney. The kidney and its adherent neoplasm are intimately fused together and cannot be separated from each other without extensive laceration, except for that peripheral nodule of kidney not as yet compressed.

The degree of kidney change in size and shape varies with the size of the tumor. A portion of kidney tissue about one-half the size of its opposite kidney is the largest amount of kidney substance remaining adherent to the tumor fused with the neoplasm in any of our patients. The amount of kidney tissue remaining varies from a portion of a pole of the kidney downward to a band of kidney tissue 1 to 2 millimeters thick where it covers the neoplasm. The surface consists of the capsule raised irregularly by rounded nodulations. The nodules vary from pea size to the size of an adult's clinched fist. The new-growth generally is firm and retains its shape when placed on a hard surface. They are gray to pink outside and only delicately vascular.

The surfaces made by sectioning are uniformly firm, fibrillar, lobulated, and gray to faint pink-yellow in split-pea size places. Lobules are from 2 to 6 centimeters in general diameter. They are separated from each other by fibrous bands. Most of the lobules are firm throughout except for isolated portions which are soft, friable, with the consistency of an infant's brain. Elsewhere they are pink to dark red in places and 4 to 6 centimeters across. These portions are soft, porous to sponge-like with compressible resistance, and moist. Although this portion is fused intimately with the gray tumor tissue it is in sharp contrast to the major portions which are gray. The soft, fluid-like places are those of compression atrophy and liquefaction necrosis.

### MICROSCOPIC PATHOLOGY

The embryonal structure of these tumors is their most distinguishing feature with a variety

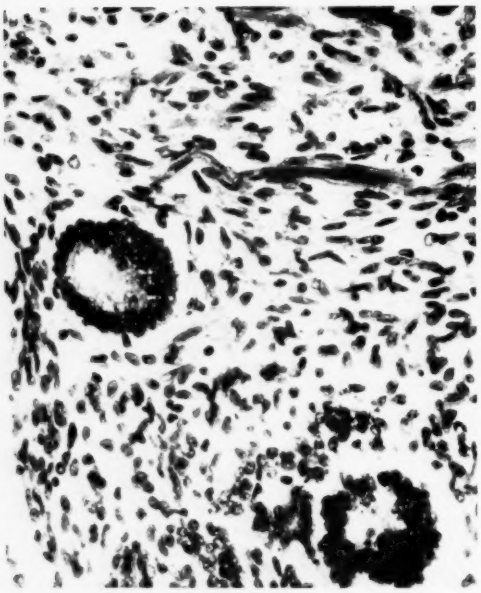

Fig. 13. Cross striated muscle fibers may also occur within the masses of undifferentiated cells adjacent to tubules. (×390.)

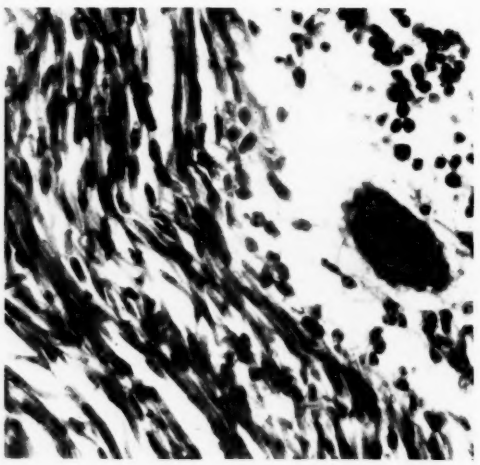

Fig. 14. Non-striated muscle is usually present in these tumors and occurs chiefly in compact masses. (×480.)

of tissue of abortive renal elements. The types of cells and amount vary in the different tumors. They are usually myxomatous tissue composed of masses of polymorphous, nucleated cells in which are imbedded gland or duct-like figures resembling uriniferous tubules which may be sparse or abundant. These embryonic tubules in a heterogeneous matrix are the most conspicuous features. There are both epithelial and connective tissue elements. The epithelial elements consist of small and large undifferentiated cells which are often spoken of as epithelial cell nests and embryonal tubules. The connective tissue elements consist of loose stroma, undifferentiated round cells, striated and non-striated muscle fibers. These elements are most irregularly mixed. The tubules are in many stages of development and usually consist of single layers of cuboid and columnar type epithelium, although several layers are occasionally present resting on a thin basement membrane. The tubules, in general, are round, but occasionally have horseshoe-shaped lumina which may be irregular in outline. The tubules may occur in dense lobular clumps separated by only a few cells or they may be present as a single tubule in solid masses of undifferentiated cells which divide rapidly. The lumen of the tubule occasionally may not be visible and other tubules in the process of growth may be indicated by a clumping of the cells in the central portions of the masses of undifferentiated cells. The chief features of these cells are their polymorphism, abundance of mitotic figures, and dense chromatin. They may have fragmented nuclei, and but little cytoplasm. The stroma between the masses of embryonal cells is myxomatous and delicately fibrous. The epithelial cell nests which stain deeply, are often sharply defined from other undifferentiated masses of cells which are more round, contain less chromatin and fewer mitoses. The fibrous bands which group the tumor cells in rather large clusters contain, in places, cells with spindle shape nuclei which are usually sparsely distributed.

Striated muscle is another interesting feature of these tumors. These fibers are best stained with phosphotungstic acid hematoxylin. Striated muscle is present in the majority of these tumors. It is present usually in clumps of fibers, but occasionally single strands of striated muscle ramify throughout

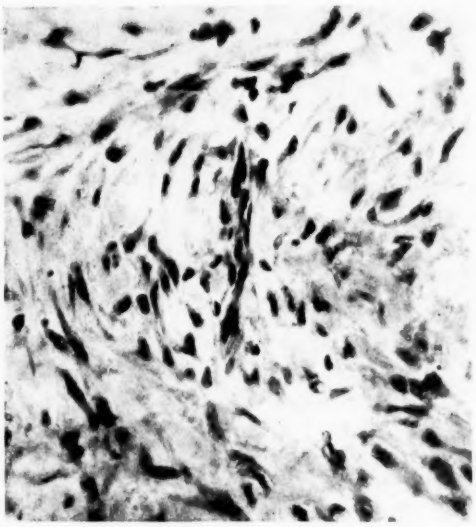

Fig. 15. A loose, spindle cell stroma is always present in some portion of these tumors. (×480.)

the epithelial cell masses. Non-striated fibers are present in all of these tumors and are usually present in compact clumps in an orderly arrangement.

Aberrant cross-striated muscle fibers have also been observed in the thyroid gland (Hirsch), and in the sino-auricular node (Yater).

Necrosis of the tumor itself is often marked. It usually is most marked where growth has been most rapid.

In the portion of the kidney not yet obliterated, where the kidney is adjacent to the tumor, the tubules are usually widely dilated.

The recurrences of tumor growths following surgical excision of the primary tumor have all been histologically similar to the original tumor structure.

Cartilage or bone was not found in any of our tumors.

### METASTASES

Extensions and metastases of these tumors are exceptional unless the original tumor is large. Regional involvement by extension is the usual method of growth. Extension metastases may occur throughout the entire abdomen, engulfing the viscera by its growth so as completely to enclose such viscera as the

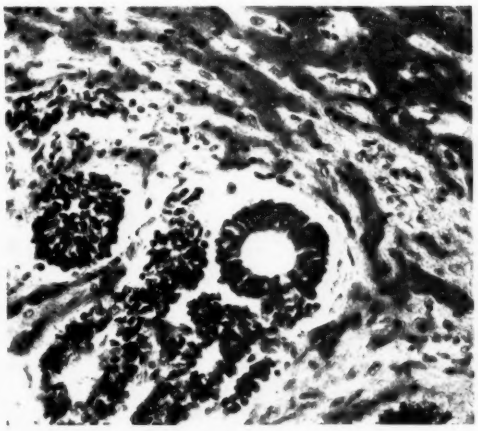

Fig. 16. Metastases in the liver. When present in the liver the metastases simulate the structure of the original tumor. (×290.)

pancreas and suprarenals. They may penetrate through the walls of the blood vessels, usually the veins, in one instance a ureter, and may extend through the diaphragm so that tumor nodules may be present on its pleural surface. Hæmatogenous extensions are predominately to the liver and occasionally to the lung. Metastases in the liver (Fig. 16) duplicate remarkably the typical new tubule formation, which tubules may be present in clumps or single tubules in a matrix identical to that of the primary tumor. Muscle fibers were not seen in the metastases. Metastases in the lungs (Fig. 17) are usually nodules 1 to 3 centimeters in diameter. They are firm, gray, and sharply-defined. These consist of undifferentiated round cells with scant chromatin.

In isolated places they retain a mass of polymorphous cells, with dense chromatin, arranged in a compact cluster, and they resemble abortive renal tubules. These extension metastases may be so huge as to compress great veins or by compression in the liver, bile cysts may result.

### SEX

As a rule the question of sex is of but little moment as an aid in making a diagnosis, so that the sex incidence is only one of academic interest. Still it is extremely interesting to note that in this series of 17 cases, 14 of them occurred in males whereas only 3 were females.

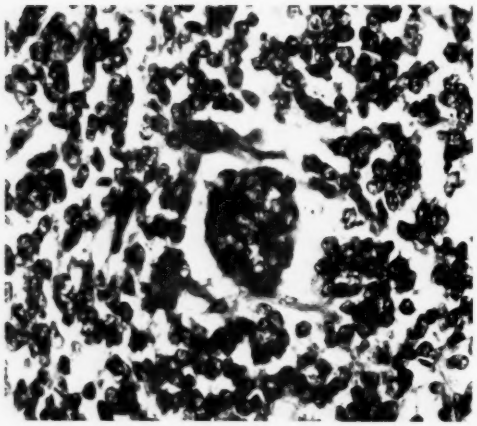

Fig. 17. Metastases in the lung. When present in the lungs the metastases consist essentially of undifferentiated cell masses with less nuclear chromatin than the cells in the primary tumor. The tubules are seldom sharply defined and are usually indicated by a clump of cells in a gland-like arrangement. (×480.)

Fig. 18. Embryonal adenosarcoma of the kidney in swine. In these tumors of swine the conspicuous feature is the abundance of tubular structures of various shapes and sizes. The tubules in swine tumors are evidently more mature than in the human. Striated muscle is seldom present, but non-striated muscle, cartilage, and bone are commonly found. (×325.)

### AGE

The oldest case in this series was 6½ years and the youngest, 3 months.

| | Cases |
|---|---|
| Under 6 months | 2 |
| 6 months to 1 year | 1 |
| 1 to 2 years | 5 |
| 2 to 3 years | 3 |
| 3 to 4 years | 1 |
| 4 to 5 years | 0 |
| 5 to 6 years | 3 |
| 6 to 7 years | 2 |

### ONSET

As a rule the time that had elapsed between the time when the symptoms were first noted and when the parents took the little patients to the doctor for examination was very short. This varied from 6 days in one case to 12 months in the longest. It was exceedingly hard to get an accurate line on the time of onset, i.e., to determine the length of time that the tumor had been present, because so many of these little patients when brought in had been ill or demonstrated symptoms for only a relatively short period of time; whereas examination revealed very large, extensive abdominal tumors so that it was quite evident that the growth had reached its large size before its presence was discovered and the patients sent in.

### PAIN

In 5 cases the patients complained of pain in the region of the tumor. In Case 7 the tumor was located on the right side and the pain complained of was on the left side.

### URINARY SYMPTOMS

*Frequency* of urination was present in only 1 case (Case 1). This symptom, however, was not very severe but had been present for 4 months.

*Hæmaturia.* Gross blood in the urine was not found. In one case (Case 2) the patient's history at the time of admission was negative on this point and the mother was told to look for blood in the urine. On patient's second admission the mother said that since leaving the hospital there had been some bloody urine, but this was *not verified.* It would seem, therefore, from a study of this series of cases, that the statement is justified that hæmaturia —gross bleeding—is rarely present in this type of tumor. Our own experience coincides with this view.

### FEVER

An increase of temperature is often found in malignant tumors of the adult. Israel drew attention to this fact many years ago. An analysis of malignant tumors in the adult by one of us (H. L. K.) showed an elevation of temperature in 11 in a series of 54 cases. But attention was drawn at that time to the fact that other conditions were present that might have been factors in the production of fever such as infections in the teeth, tonsils, and sinuses.

In this group of 17 cases, fever was present in 9 cases.

### GENERAL SYMPTOMS

| | Cases |
|---|---|
| Palpable tumor | 17 |
| Fever | 9 |
| Pain in abdomen | 6 |
| Loss of appetite | 4 |
| Loss of weight | 3 |
| Constipation | 3 |
| Irritability | 2 |
| Vomiting | 2 |
| Frequency of urination | 1 |

### SIDE INVOLVED

Equally interesting was the fact that although it is generally assumed that right sided kidney lesions are more common than left sided lesions, we find quite the reverse situation in our studies, in that in 10 of the 17 cases the malignant tumor was found on the left side and in 5 on the right. In 2 cases (Cases 4 and 12), there was a bilateral involvement, an exceedingly rare finding as far as we can tell, judging from case reports in the literature (Fig. 7, Case 12). Whether this was due to a primary tumor developing in the remaining kidney after the decapsulation or whether the growth was metastatic is a question which we feel we cannot positively answer.

| | Cases |
|---|---|
| Left | 10 |
| Right | 5 |
| Bilateral | 2 |

### PRESENCE OF TUMOR

In every one of these cases a palpable tumor was present. In all but one, the presence of the tumor was directly responsible for the patients being brought to the physician. As a rule, the tumor was discovered accidentally either by the mother or a nursemaid, and therefore was the first symptom. Furthermore, a careful review of these cases showed that the presence of tumor was about the only symptom of which they complained. In only 3 of these patients was there a direct history of trauma (Cases 11, 14, and 16).

### URINALYSIS

Albumin was present in 7 cases; microscopic blood was found in only 1 case. In 1 case the presence of sugar was noted. When this patient entered the hospital the urine was negative. Re-entering on account of extensive abdominal metastases, particularly in the region of the liver, an examination of the urine revealed the presence of sugar. The metastatic masses involved the liver. In 3 cases a few red blood cells were found in the urinary sediment.

| | Cases |
|---|---|
| Albumin | 7 |
| Leucocytes | 5 |
| Red blood cells | 3 |
| Casts | 2 |
| Microscopic blood | 1 |
| Sugar | 1 |

The Wassermann test was negative in all cases.

### BLOOD COUNTS

In every case there was present a very definite evidence of a secondary anæmia. This was most marked in Case 2, in which the red count was 2,000,000. There was an increase in the white blood cells in 8 cases. The highest count was 28,650.

### CYSTOSCOPY AND URETERAL CATHETERIZATION

The problems of diagnosis and the study of renal function in these cases do not differ from those in the adult. All these cases should be subjected to cystoscopic examination and ureteral catheterization for purposes of making a pyelogram and in order to determine the function of the opposite kidney. An intravenous pyelogram may be made before the cystoscopic examination is carried out and, if necessary, this can be checked with pyelograms from below.

The cystoscopic examination when done was negative.

In one case the pyelogram was practically normal outside of showing a few minor changes in the calyces due to clubbing, but there was no compression and filling defect such as one generally sees in malignant tumors.

Because the tumors were large and completely filled the kidney pelvis, many of the cases showed so complete a blocking at the uteropelvic junction, that no pyelogram could be obtained.

This type of finding may at times be confused with a block at the ureteropelvic junction due to a large hydronephrosis associated with kink and thereby preventing a filling of the kidney pelvis. In one of our cases, in which the tumor was rather soft and elicited a feeling of slight fluctuation, the possibility of hydronephrosis was considered.

The pyelogram is not only of value in differentiating various types of kidney lesions, but it is also valuable in differentiating lesions of the liver and spleen as well as those rare cases of tumors of the adrenal, hydronephrosis, solitary cyst of the kidney, and congenital polycystic disease, although solitary cyst of the kidney and congenital polycystic disease rarely call for differentiation in early life. Finally, the importance of determining the presence of a second kidney and of estimating its function before nephrectomy is just as important in children as it is in adults. A point that should be stressed is the possibility of bilateral involvement, inasmuch as we found this complication in 2 of 17 cases, that is, nearly 12 per cent.

## SUMMARY

1. A series of 17 cases of this supposedly rare and unusual type of kidney tumor is reported.

2. Some of the cases were incorrectly diagnosed and a subsequent study by us revealed the true nature of the tumor.

3. This type of tumor is the most common tumor found in swine.

4. A careful histological study of specimens is convincing that this growth is the common tumor of infancy and childhood.

5. Hæmaturia, so common in the adult, is rarely, if ever, present in children.

6. Most of the patients are seen when the tumors have reached an enormous size.

7. The prognosis is bad; 16 of our 17 patients died.

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# THE INFLUENCE OF CERVICAL PARAVERTEBRAL ANÆSTHESIA UPON THE PULSE RATE DURING OPERATIONS UPON THE TOXIC THYROID GLAND[1]

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OF late years the use of iodine in the pre-operative preparation of patients suffering from toxic goiter has done much to rid the mind of the surgeon of fear of cardiac collapse during operation and the danger of the so-called thyroid crisis following operation. In operations performed under local infiltration anæsthesia or one or other of the various inhalation anæsthetics, the pulse becomes more rapid during operation and the necessary manipulations of the operative procedure place an added strain upon the already overstimulated cardiac mechanism which may result in a more or less stormy postoperative convalescence even though cardiac collapse does not occur. A form of anæsthesia, therefore, which will control this cardiac hyperexcitability even temporarily should be of benefit; and to demonstrate that cervical paravertebral anæsthesia appears to accomplish this end will be the object of this paper.

## THE CARDIAC ACCELERATOR MECHANISM

The impulses which control the rate of the heartbeat reach the heart from without through the sympathetic and parasympathetic nervous systems—the sympathetic conveying the accelerator and the parasympathetic the depressor impulses. The fibers of the sympathetic system through which these accelerator impulses are conveyed arise at various levels from that portion of the sympathetic ganglionated cord which extends from the superior cervical to the fourth thoracic ganglion and may, for the purpose of this discussion, be divided into three main groups, an upper, middle, and lower. The upper group is formed by the superior and middle cervical cardiac branches of the sympathetic and is the group with which we are principally concerned. The middle group includes the lower cervical cardiac nerve which arises from the lower cervical ganglion and the lower group takes in the upper thoracic cardiac nerves which have lately been described by Kuntz and Morehouse (Figs. 1 and 2).

The superior cervical cardiac nerve arises from the lower portion of the superior cervical ganglion or the sympathetic cord immediately below it and passes downward on either side of the neck lying on the surface of the longus colli muscle. On the right side the nerve ultimately reaches the deep cardiac plexus and on the left, after crossing over the arch of the aorta behind the innominate artery joins the superficial cardiac plexus (Figs. 1, 3, and 4).

The middle cervical cardiac nerve is a variable quantity. In some cases it is absent on one side or both and in this event its function is taken over by the superior cardiac nerve. When present it may arise from the middle cervical ganglion or, if this is absent, from either the sympathetic cord immediately below the superior cervical ganglion or from the superior cervical ganglion itself (Figs. 1, 3, and 4). In any event the nerve of each side enters the deep cardiac plexus as it passes over it.

It can thus be seen that a considerable amount of the cardiac accelerator stimulation is carried by nerves which have their origin in the upper portion of the neck in close proximity to the points of emergence of the four upper peripheral cervical nerves and to the transverse processes of the four upper cervical vertebræ. Consequently, the injection of an anæsthetic solution around these nerves or around their points of origin from the superior cervical sympathetic ganglion and upper part of the sympathetic cord should theoretically anæsthetize them temporarily and result in the cutting off of a greater or lesser amount of the accelerator impulses reaching the cardiac plexuses. A considerable portion of the hyperexcitability of the sympathetic system due to the altered thyroid secretion thus being cut down or abolished, the moderator influence of the parasympathetic

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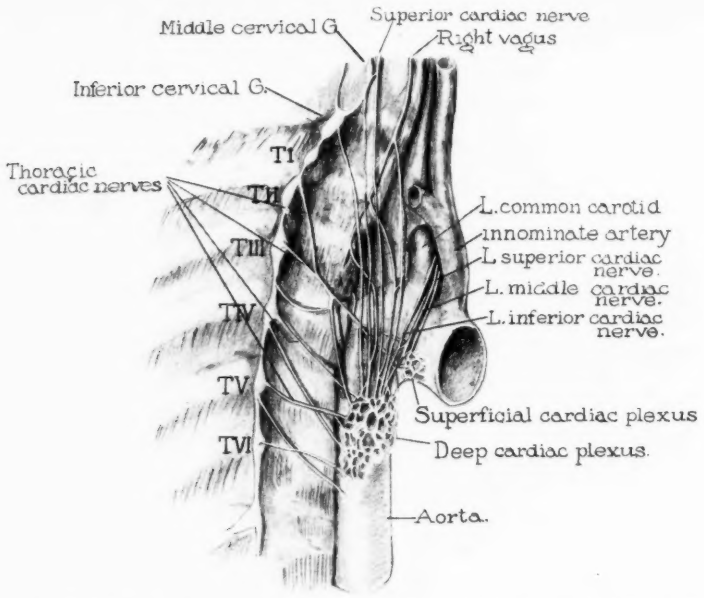


Fig. 1. The nerves entering the cardiac plexus from the right side. (After Kuntz and Morehouse.)

should be able to counterbalance, at least in part, the accelerator impulses reaching the heart from the lower cervical and upper thoracic sympathetic nerves and a slowing of the pulse rate result.

THE FASCIAL RELATIONS OF THE UPPER CERVICAL SYMPATHETIC GANGLION AND SYMPATHETIC CORD

The upper cervical sympathetic ganglion appears to be very closely related to many extremely important structures in the neck, anæsthetization of which would be very dangerous. The most important of these structures is the pneumogastric nerve. The ganglion is situated behind the carotid vessels and the internal jugular vein and is crossed obliquely by the pneumogastric nerve (Fig. 4). These structures are, however, enclosed in the carotid sheath and posterior to this there is a layer of connective tissue, the sympathetic sheath, which covers the surface of the upper ganglion and cord and still further separates it from the structures in front of it (Figs. 5 and 6). This sheath is present in front and lateral to the ganglion as well as behind it and at its anteromesial and posterolateral portions blends with the fascial layers of the prevertebral muscles and deep muscles of the neck. Enclosed within this sheath is a mass of loose areolar tissue in which are situated the superior ganglion and its branches. The upper cervical nerves, as they go to their definitive points of distribution, pass through this tissue, and it is in this tissue that the anæsthetic is placed in paravertebral anæsthesia. The main branches of the ganglion which are of interest in this situation are the rami communicantes between it and the upper cervical nerves (Figs. 3, 4, and 7). These branches, if temporarily divided as it were, through paralysis by a local anæsthetic should serve to isolate the superior ganglion still further from the structures with which it is connected, and render it still more impossible for it to exert its accelerator function on the cardiac beat. In other words the injection of an anæsthetic solution into the loose connective tissue lying in front of, and lateral to, the transverse processes of the upper four cervical vertebræ

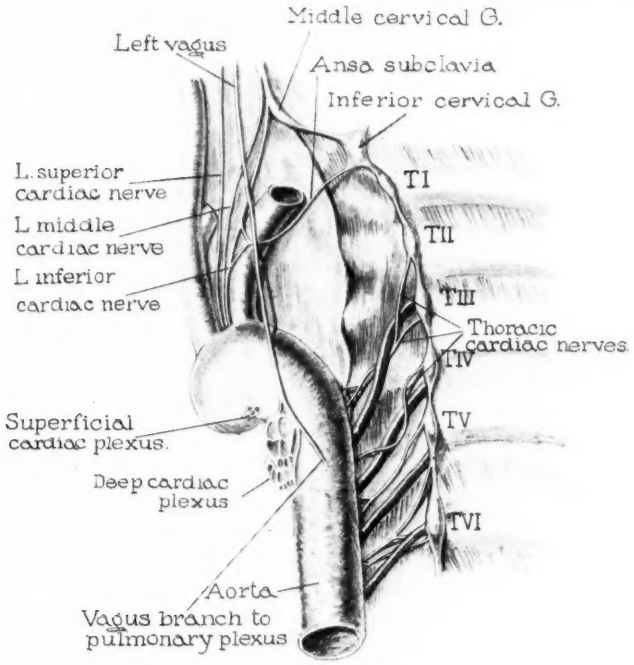


Fig. 2. The nerves entering the cardiac plexus from the left side. (After Kuntz and Morehouse.)

should result in what to all intents and purposes would be a temporary resection of the upper cervical sympathetic ganglion and the upper portion of the cervical sympathetic cord together with the superior and a great portion of the middle cervical cardiac nerves.

The procedure of sectioning the sympathetic cord below the superior cervical ganglion to prevent ulceration of the cornea in exophthalmic goiter was suggested and performed by Edmunds in 1895. In the following year Jaboulay repeated the procedure believing that it would benefit the symptoms of exophthalmic goiter. Jonnesco, who first reported on the subject in 1896, at first resected the upper sympathetic ganglion and later extended the procedure to the entire cervical cord including the middle and inferior ganglia for the relief of symptoms of toxic goiter. These men and others later reported amelioration and in some instances symptomatic cure of toxic goiter patients by these procedures.

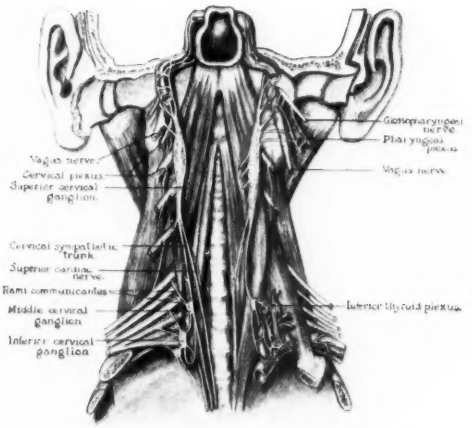


Fig. 3. Cervical sympathetic system showing the ganglia, the connections with the peripheral nerves and its peripheral branches. (After Toldt.)

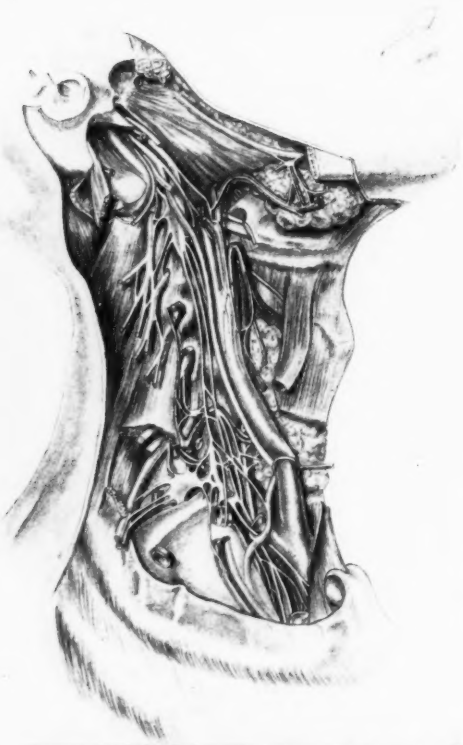

Fig. 4. The sympathetic nervous system of the right side of the neck showing the superior and middle cardiac branches of the sympathetic and the connection of the upper cervical sympathetic ganglion with the peripheral nerves. (After Jonnesco.)

It is therefore evident that a method of anæsthesia which would temporarily inhibit the increased action of the accelerator portion of the sympathetic system should show, as a result of this action, a diminution in the frequency of the pulse while the anæsthetic is active and with this, less shock resulting from the operation and less reaction following it.

In order to determine the behavior of the pulse as to its frequency during operation on toxic goiter, a record of the beat was taken every 5 minutes either from the time the patient entered the operating room or from the time the actual operation was begun and continued until the close of the operation. Subsequently the rate of the pulse was recorded graphically (Fig. 8).

Fig. 5. The sympathetic system of the left side of the neck. Note particularly the fascia covering the upper cervical ganglion and its branches and separating it from the carotid vessels. (After Jonnesco.) It is beneath this fascia that the anæsthetic is deposited.

Although it was my impression that during operations under infiltration anæsthesia there was a tendency for the pulse rate to rise either throughout the operation or reach its peak at the time of actual division and removal of the anterior portions of the thyroid from that portion of the gland to be left on either side; two operations were performed under infiltration anæsthesia, the patient being prepared exactly as for paravertebral anæsthesia and the pulse rate recorded and subsequently graphs made. These showed, as was expected, practically a continuous rise in pulse rate throughout the early and difficult portions of the operation (Fig. 8 A and B).

Observations were then made on a series of 18 cases of goiter exhibiting toxic symptoms of varying degrees of severity which were operated upon under cervical paravertebral anæsthesia. The cases represented a varying symptomatology so far as the presence of eye signs and tachycardia were concerned as well as the duration of symptoms.

The graphs obtained (Fig. 8 C to T) appear to fall into two main divisions (Fig. 8 C to P

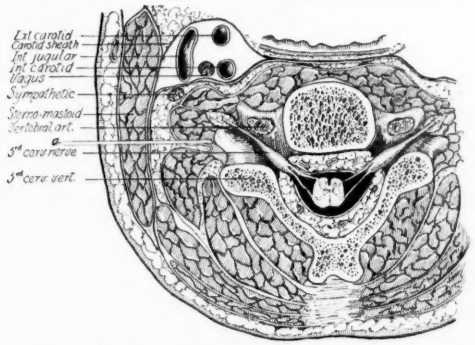


Fig. 6. Cervical plexus block by the lateral route. Cross section of neck at level of third cervical vertebra showing direction of needle, *a*. Note the comparatively thin layer traversed by the needle and the distance of the large blood vessels from the path of the needle and site of injection and their protection by the carotid sheath. Note also the position of the sympathetic cord and its relation to the third cervical nerve. (Modified from Labat.)

and Q to S), with a graph (Fig. 8 T) which seems difficult to interpret.

In the first group (Fig. 8 C to P) is represented a series of cases of goiter showing symptoms indicative of varying degrees of hyperthyroidism. Some were acute cases and other cases of long standing. Some showed definite exophthalmos, others did not. One case had passed through two attacks of auricular fibrillation one of which had been preceded by an attack of auricular flutter. There were different changes in the percentage of free hydrochloric acid in the stomach contents varying from practically normal to absence of free hydrochloric acid. The essential point, however, is that all showed symptoms of hyperthyroidism of some type. The postoperative examination of the glands removed at operation showed histological changes varying from almost pure adenoma to practically pure hyperplasia.

The pulse graphs exhibit a remarkable similarity. There is a rapid rise in pulse rate during the administration of the paravertebral anæsthesia comparable to the rise in pulse rate shown in the cases operated upon under infiltration anæsthesia. During this period the patient is disturbed by the turning of the head, introduction of the anæsthetic, and finally by being draped for the operation. By the time draping is completed the patient is

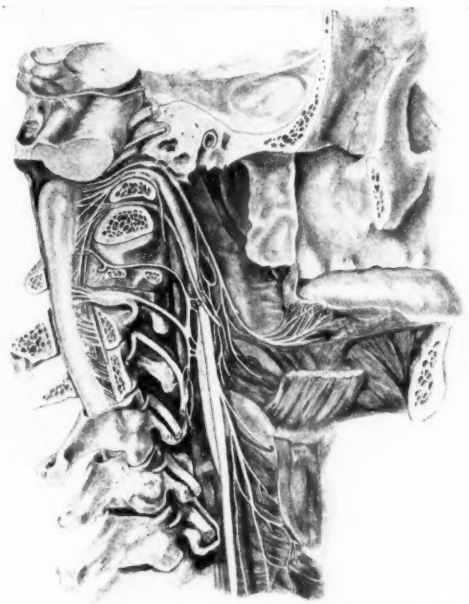

Fig. 7. The sympathetic system in the neck showing the connections of the upper cervical sympathetic ganglion with the peripheral nerves. (After Spalteholz.) Note the close relation of the ganglion to the transverse processes of the cervical vertebræ.

anæsthetized and with the beginning of the operation the pulse begins to fall in frequency and on the average reaches its lowest rate at the time the thyroid gland is being delivered, divided, and removed. If the operation is performed slowly there is a slight rise in pulse rate which occurs on an average of 35 or 40 minutes after the start of the operation which I interpret as being due to the beginning recovery of the sympathetic ganglion and cord from the effects of the anæsthesia and the renewal of the transmission of accelerator impulses to the heart. After the return of the patient from the operating room the pulse rises, but the postoperative rise in pulse rate is less high, and the convalescence smoother, than in cases operated upon by other methods of anæsthetization.

The second group of graphs (Fig. 8 Q to S) is taken from cases exhibiting cardiac irregularity or auricular fibrillation at the time of operation. These graphs are, with our present knowledge, practically impossible to interpret.

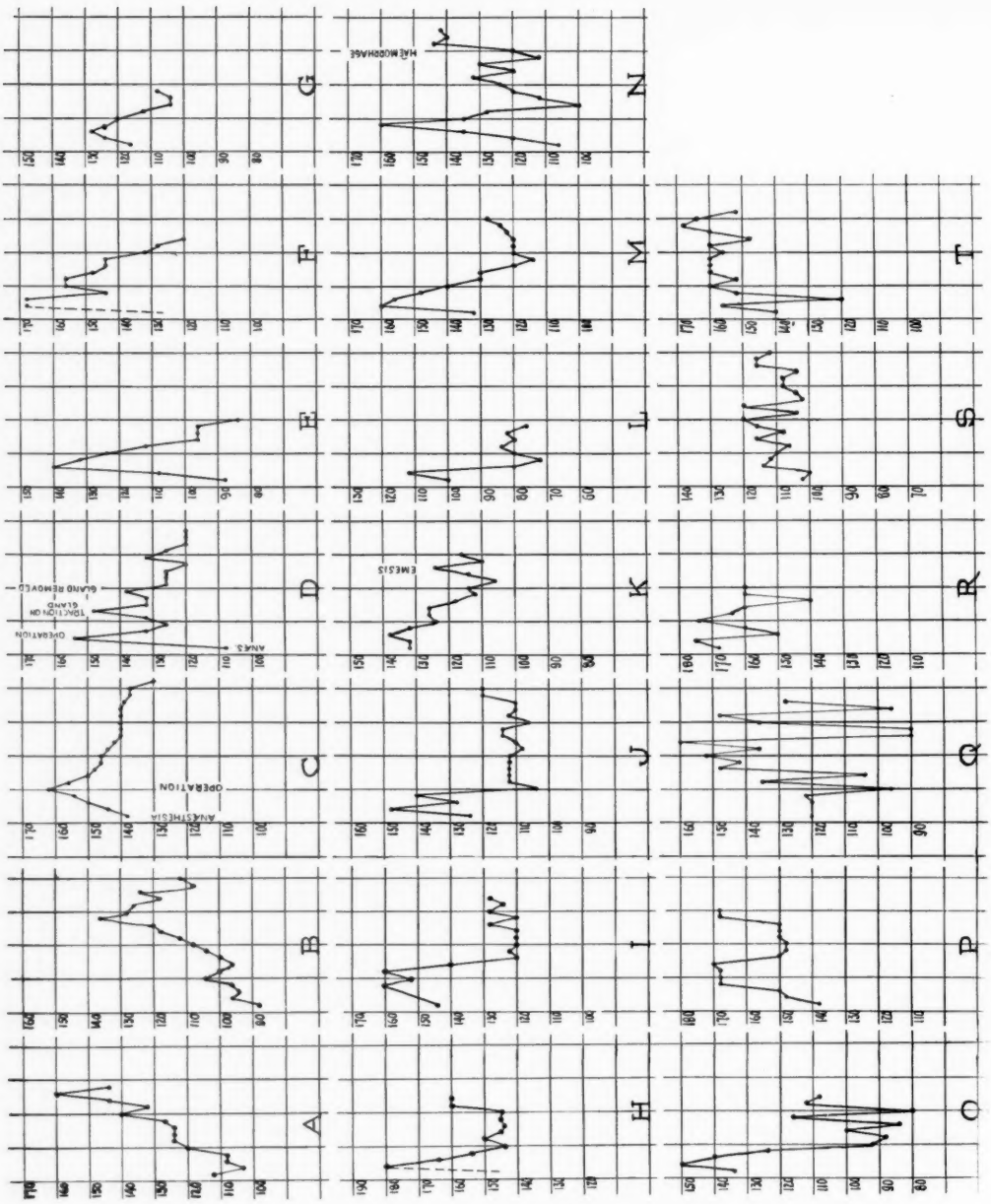


Fig. 8. Graphs of the pulse rate during operations for toxic goiter. The distance between dots represents a time interval of 5 minutes. The figures at the left represent the frequency of the pulse.

It is my belief that the apparent rise in rate is due to the fact that more beats are coming through to the wrist and that though the pulse is actually more rapid, the heart action is in reality of better quality; but at present there is no evidence that this is the true conclusion and further investigation of similar cases will be necessary before this hypothesis can be either proved or disproved.

Graph T, Figure 8, is an extremely interesting one as it differs from any of the other graphs obtained. It will be noted that the sharp rise in rate during the administration of the anæsthetic corresponds to the rise seen in graphs C to P. This is followed by the rapid fall in rate characteristic of these same graphs; but this is followed by an immediate rise to a high rate which is maintained throughout the remainder of the operation. Gastro-intestinal symptoms in this case were more marked than in any of the other cases; which would point to a condition of hyperexcitability of the sympathetic chain below the area of anæsthetization. This hyperexcitability acting through the lower cervical and upper thoracic sympathetic nerves to the cardiac plexuses might be sufficient to maintain the pulse at a high level as they would not be anæsthetized. The primary drop of short duration may be explained by an evanescent preponderance of the parasympathetic when part of the sympathetic hyperexcitability was suddenly removed by the anæsthetization of the superior and middle sympathetic cardiac nerves.

## CONCLUSIONS

1. Cervical paravertebral anæsthesia, in addition to anæsthetizing the upper cervical nerves also anæsthetizes the upper cervical sympathetic ganglion and the upper part of the sympathetic cord.

2. This anæsthetization renders the superior and middle cervical cardiac nerves incapable of transmitting to the heart the increased accelerator impulses caused by the hypersensitization of these nerves and the moderator impulses of the vagus reach the heart opposed only by the accelerator impulses through the lower cervical and upper thoracic cardiac branches of the sympathetic which are usually not strong enough to overcome the vagus action completely and the pulse rate falls. Consequently—

3. During the operation of subtotal thyroidectomy for hyperthyroidism, cervical paravertebral anæsthesia exerts a definite action toward slowing the rate of the pulse.

4. Owing to the fact that under paravertebral anæsthesia cardiac shock is less marked, the operative procedure does not diminish the patient's already weakened cardiac reserve and the postoperative course is smoother with relatively less cardiac reaction than with other types of anæsthesia.

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# AN HISTOLOGICAL STUDY OF THE PERIVAGINAL FASCIA IN A NULLIPARA[1]

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THOUGH much thereon has been written, gynecologists still differ widely in their opinions about the pelvic fascia, especially about that portion of it which surrounds the vagina. Some contend that there is a layer of fascia between the wall of the vagina and the walls of the urethra, bladder, and rectum. They believe that obstetric injury to this fascia is the fundamental cause of cystocele, rectocele, and urethrocele. Furthermore, when operating for these conditions they demonstrate by dissection a layer of pallid tissue several millimeters thick, which lies just beneath the vaginal mucosa, and term it fascia. On the contrary, others deny the existence of such a fascia. They offer various explanations concerning the cause of the conditions mentioned, and contend that successful vaginal plastic surgery is not essentially based on the utilization of fascia.

In view of the fact that there is such a wide difference of opinion, and since the prevalent opinions are based on the findings in gross dissections or on microscopic studies of material from abnormal subjects, it has seemed logical to resort to an histological cross section study of the tissues in and between the walls of the vagina, bladder, urethra, and rectum in a normal nullipara, for only by means of such studies will it be possible to establish important fundamental facts concerning their character and interrelationship under normal conditions. It is obvious that an accurate knowledge of the normal structure of the tissues in and about the vaginal wall is essential to a clear understanding of the etiology and surgical treatment of cystocele, rectocele, and urethrocele. A careful search through the literature has failed to reveal any previous attempt of a similar nature with the exception of a study by Spaulding of sections from the vesicovaginal septum in which the author has failed to state whether the subject from whom the material was taken was nulliparous or multiparous.

Before entering into a discussion of any part of the pelvic fascia, it is important to agree upon a definition of the term fascia which will be acceptable to histologists. Obvious as this may seem, it is all the more important since many gynecologists are inclined to include under the term fascia tissue which has the gross appearance of fascia but which histologically is composed principally of smooth muscle with a relatively small amount of interfascicular connective tissue. A perusal of the literature reveals no definition clearer and more comprehensive than that of Piersol who states: "Connecting the various muscles and uniting them into groups, and also surrounding the entire musculature of the body and separating it from the deeper layers of the integument, are sheets of connective tissue known as fascia. These sheets are by no means isolated portions of connective tissue, but are rather to be regarded as parts of the general interstitial connective tissue network which traverses all parts of the body, thickened to form more or less definite sheets standing in relation to neighboring organs. The density of the sheets varies greatly; in some regions they are imperfectly developed, while in others they form dense, glistening sheets." It is obvious that this definition does not permit the inclusion under the term fascia of tissue in which smooth muscle predominates, regardless of its gross appearance.

The fibrous interstitial connective tissues of the body may be divided into two classes: (1) loose fibrous, or areolar tissue, which occurs throughout the body wherever the opposed parts, although connected, enjoy considerable mobility. Familiar examples are the sheets or tracts of yielding connective tissue which lie beneath the skin and the underlying fascia, that unite the muscles, and that assist in keeping the viscera in place. In this type of tissue the variable bundles of white fibers are loosely and irregularly disposed, crossing in all directions and enclosing correspondingly

[1]Read by invitation before American Gynecological Society, May 20, 1930.

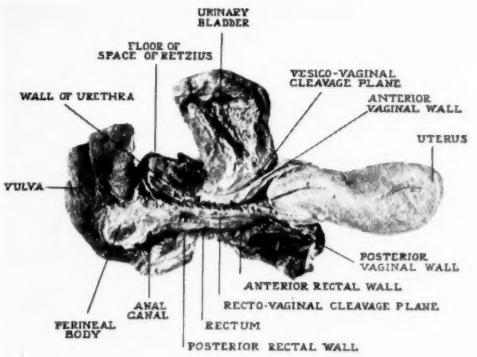


Fig. 1. Photograph of the fixed gross specimen from which the microscopic sections were made. Note the loose attachment of the vaginal wall to bladder wall and rectal wall and the firm attachment of the anterior vaginal wall to the wall of the urethra.

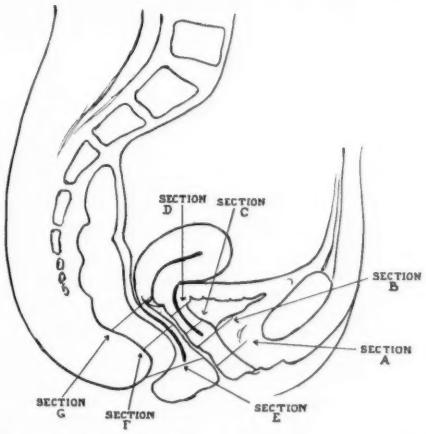


Fig. 2. Microscopic cross sections were made at the levels indicated in the above diagram.

irregular clefts. The elastic fibers form a network of highly refracting threads which, in section and teased preparation, are more or less wavy and curled. The cellular constituents of the normal tissue are relatively inconspicuous, but here and there the fixed connective tissue cells are seen as spindle shaped or irregular plate-like bodies and the free cells usually as rounded forms. In the inter-fascicular spaces are the tissue fluids, and in the fluids the free cells migrate. (2) Dense fibrous tissue which owes its characteristics to the more compact and orderly arrangement of the bundles of white fibers. Although the individual fibers are no thicker than in areolar tissue, they are grouped into larger bundles and held more closely together by the interfibrillary cement or ground substance. The bundles are disposed with greater regularity as intimately felted bands which form fibrous sheets termed fascia. (Piersol.)

In view of the fact that the constituent elements of loose and dense fibrous tissue are alike, and since the significant difference between the two types is found in the arrangement of the white fibers, it seems logical and desirable to speak of two types of fascia: an areolar type which surrounds and aids in the maintenance of the viscera, blood vessels, and nerves in their normal positions; and a denser type which sheathes and unites the voluntary muscles of the body. My conclusions have been based upon such a classification.

The specimen (Fig. 1) upon which the present study has been based consisted of the uterus and vagina; the bladder and urethra; the rectum and anal canal; the perineum and vulva; and parts of the levatores ani muscles. It was removed from the body of an exceptionally well formed and developed nullipara, 27 years of age, 16 hours after a sudden death caused by a thoracic injury. Immediately after removal, the specimen was placed in formalin for a period of 7 days, and an attempt was then made to bisect it in the sagittal plane of the body. Fortunately, the section passed slightly to the right of the sagittal plane with the result that the urethra remained intact in the left half of the specimen which was used for the histological examination. Cross sections were made at a right angle to the long axis of the vaginal canal at two levels through the anterior vaginal wall and the wall of the urethra; at two levels through the anterior vaginal wall and the adjoining wall of the bladder; at one level through the posterior vaginal wall and the wall of the rectum (Fig. 2). The microscopic sections were stained by: (1) eosin and hematoxylin; (2) van Giesen for connective tissue; (3) elastic tissue stain.

An examination of the gross specimen (Fig. 1) reveals two points of practical impor-

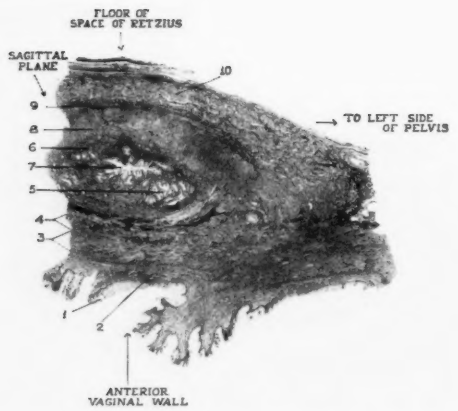


Fig. 3. Low power photomicrograph of cross section *A* which passes through the anterior vaginal wall and the urethral wall at a level just above the point at which the urethra penetrates the superior layer of the triangular ligament of the perineum. *1*, Stratified squamous epithelium of vaginal mucosa; *2*, fibro-elastic tunica propria of vaginal mucosa; *3*, muscular coat of vaginal wall; *4*, muscular coat of urethral wall; *5*, urethral glands; *6*, tunica propria of urethral mucosa; *7*, urethral mucosa; *8* and *9*, muscular coats of urethral wall; *10*, extrinsic voluntary muscle fibers of urethral wall.

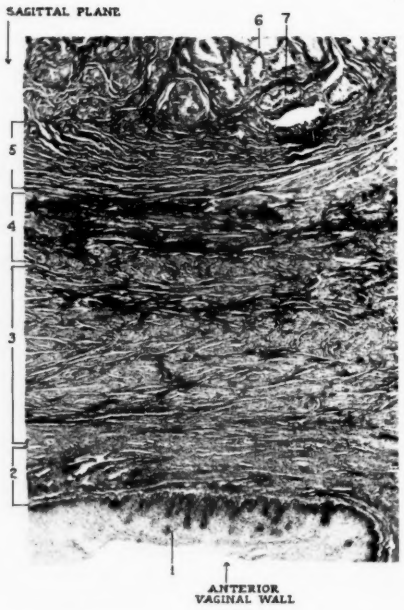


Fig. 4. High power photomicrograph of vaginal wall and urethral wall from cross section *A*. *1*, Stratified squamous epithelium of vaginal mucosa; *2*, fibro-elastic tunica propria of vaginal mucosa; *3*, muscular coat of vaginal wall; *4*, muscular coat of urethral wall; *5*, tunica propria of urethral mucosa; *6*, epithelium of urethral mucosa; *7*, urethral gland.

tance. If the anterior vaginal wall is examined throughout its extent it will be found that in its lower part, where it is in contact with the urethral wall, the union of the two walls is a very firm one with no natural line of cleavage between them, while in its upper part, where it is in contact with the wall of the bladder, the union between the two walls is a very loose one. The vaginal wall and the bladder wall are loosely held together by a layer of areolar connective tissue. Bissell and Rawls have emphasized the practical importance of entering and following this avascular line of loose attachment when separating the vaginal wall from the bladder wall in operations for cystocele. By following it the vaginal wall can be kept intact. If the posterior vaginal wall is examined throughout its extent, it will be found to be very loosely attached to the wall of the rectum from above downward until the point at which the rectum begins to turn backward to become the anal canal is reached. At that point the rectal and vaginal walls become very firmly united. This avascular line of loose attachment is similar to the one between the vaginal wall and the wall of the bladder. Between the vaginal wall and the walls of the bladder and rectum there is a natural line of cleavage, while there is no such line between the anterior vaginal wall and the wall of the urethra.

### EXAMINATION OF MICROSCOPIC SECTIONS

Section A (low power photomicrograph, Fig. 3, and high power photomicrograph, Fig. 4) is a cross section through the anterior vaginal wall and the walls of the urethra at a level slightly above the point at which the urethra penetrates the superior layer of the triangular ligament. An examination of the section from below upward reveals the mucosa of the anterior vaginal wall which is composed of a layer of stratified squamous epithelium and a fibro-elastic tunica propria. Above the vaginal mucosa is the muscular coat of the

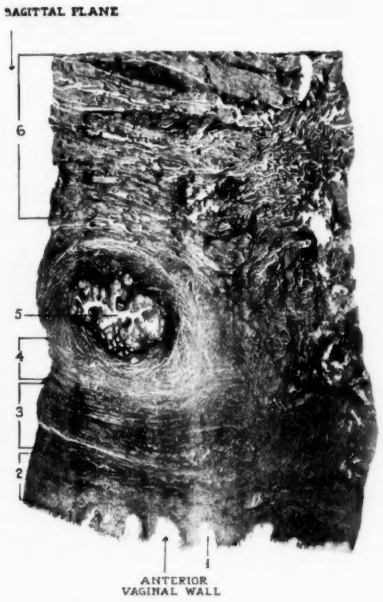


Fig. 5. Low power photomicrograph of cross section *B* which passes through the anterior vaginal wall, the wall of the urethra, and part of the adjoining bladder wall at a level where the urethra is passing through the bladder wall. *1*, Stratified squamous epithelium of vaginal mucosa; *2*, fibro-elastic tunica propria of vaginal mucosa; *3*, muscular coat of vaginal wall; *4*, muscular coat of urethral wall; *5*, urethral canal; *6*, part of muscular coat of bladder.

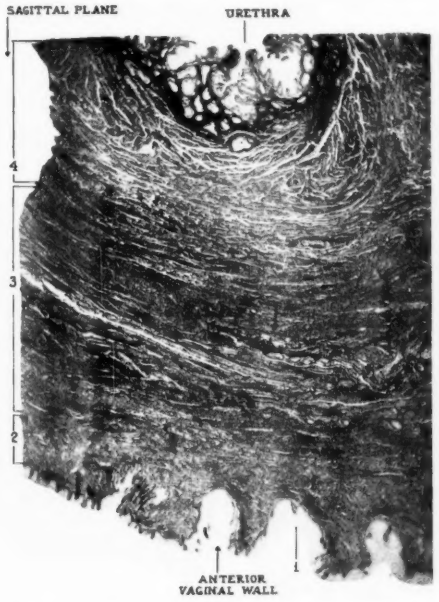


Fig. 6. High power photomicrograph of anterior vaginal wall and urethral wall from cross section *B*. *1*, Stratified squamous epithelium of vaginal mucosa; *2*, fibro-elastic tunica propria of vaginal mucosa; *3*, muscular coat of vaginal wall; *4*, muscular coat of urethral wall.

vaginal wall, the smooth muscle fibers of which are arranged in an inner circular and an outer longitudinal layer. Above the muscular coat of the vaginal wall is the muscular coat of the anterior urethral wall with its smooth muscle fibers arranged in an outer circular and an inner longitudinal layer. Adjoining the muscular coat of the urethral wall is the urethral mucosa which is composed of a mixed type of urethral epithelium and a fibro-elastic tunica propria. Above the lumen of the urethra is the posterior urethral wall, and above it a layer of extrinsic voluntary muscle fibers which have extended upward from the compressor urethræ muscle. Beyond the zone of voluntary muscle is a thin layer of fibrous tissue. It is a noteworthy fact that in this section there is no tissue in the wall of the vagina or in the wall of the urethra which is termed fascia by histologists. Certainly, there is no fascia between the wall of the vagina and the wall of the urethra, since the muscular coat of one fuses with the muscular coat of the other. An identical condition has been found in a similar section from another body which was primarily prepared for a study of the urethral epithelium, but in which the walls of the urethra and vagina are intact and in a normal relationship. In section A, a little below the junction of the muscular coat of the vagina and that of the urethral wall, there are several streaks where the stain has been unusually intense. This might lead one to believe that the tissue so stained is fascia, but the microscopic examination shows it to be intensely stained smooth muscle.

Section B (low power photomicrograph, Fig. 5, and high power photomicrograph, Fig. 6) is a cross section through the anterior vaginal wall, the walls of the urethra, and part of the wall of the bladder at a point where the urethra passes through the bladder wall. An

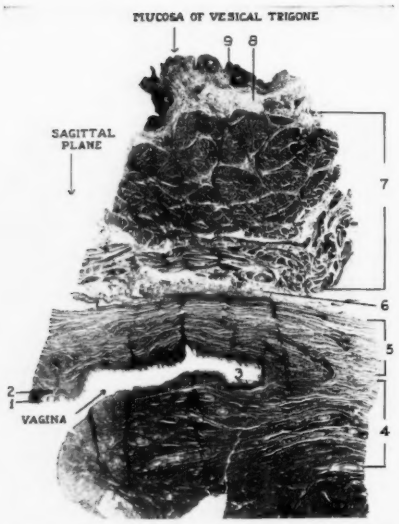


Fig. 7. Low power photomicrograph of cross section *C*, which passes through the anterior vaginal wall and the bladder wall at the midpoint of the vesical trigone. *1*, Stratified squamous epithelium of vaginal mucosa; *2*, fibro-elastic tunica propria of vaginal mucosa; *3*, left side of vaginal canal; *4*, muscular coat of posterior vaginal wall; *5*, muscular coat of anterior vaginal wall; *6*, vesicovaginal layer of areolar fascia; *7*, muscular coat of bladder wall; *8*, tunica propria of vesical mucosa; *9*, transitional epithelium of vesical mucosa.

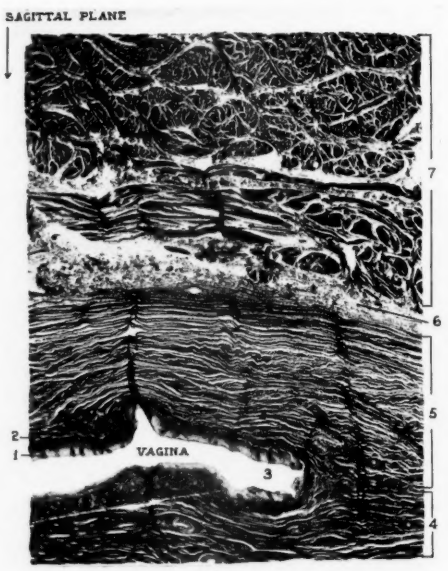


Fig. 8. High power photomicrograph of anterior vaginal wall and adjoining bladder wall from cross section *C*. *1*, Stratified squamous epithelium of vaginal mucosa; *2*, fibro-elastic tunica propria of vaginal mucosa; *3*, left side of vaginal canal; *4*, muscular coat of posterior vaginal wall; *5*, muscular coat of anterior vaginal wall; *6*, vesico-vaginal layer of areolar fascia; *7*, muscular coat of bladder wall.

examination of the section from below upward shows the vaginal mucosa composed of a layer of stratified squamous epithelium and a fibro-elastic tunica propria, above which is the muscular coat of the vaginal wall. Above the smooth muscle of the vaginal wall is found the muscular coat of the urethra, and above this the mucosa of the urethra which is composed of a mixed type of epithelium and a fibro-elastic tunica propria. Above the urethral canal is the posterior urethral wall, and above that the smooth muscle of the bladder wall. As in section A, there is no tissue in the wall of the vagina or in the wall of the urethra which is termed fascia by histologists. In this section also there is no fascia between the vaginal wall and the urethral wall.

Section C (low power photomicrograph, Fig. 7, and high power photomicrograph, Fig. 8) is a cross section through the anterior vaginal wall and the adjoining wall of the bladder at the midpoint of the vesical trigone. It also includes part of the posterior vaginal wall. It is to be noted that the section extends well beyond the left side of the vagina. An examination of the section from below upward reveals part of the posterior vaginal wall above which can be seen the lumen of the vagina. The mucosa of the anterior vaginal wall consists of a layer of stratified squamous epithelium and a narrow fibro-elastic tunica propria above which is the muscular coat of the vagina. The muscle fibers of this coat are arranged principally in a circular layer. Piersol points out the fact that the classical arrangement of the muscle fibers of the vaginal wall in an inner circular and an outer longitudinal layer is not always encountered. The arrangement of the smooth muscle in this section may therefore be considered normal. Above the muscular coat of the vaginal wall there is a thin layer of areolar connective tissue, and above that is the muscular coat of the bladder wall with the bundles of muscle

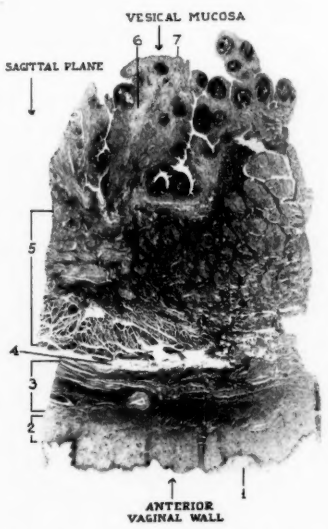


Fig. 9. Low power photomicrograph of cross section *D* which passes through the anterior vaginal wall and the bladder wall at a point just below the vesicocervical junction. *1*, Stratified squamous epithelium of vaginal mucosa; *2*, fibro-elastic tunica propria of vaginal mucosa; *3*, muscular coat of vaginal wall; *4*, vesicovaginal layer of areolar fascia; *5*, muscular coat of bladder wall; *6*, tunica propria of vesical mucosa; *7*, epithelium of vesical mucosa.

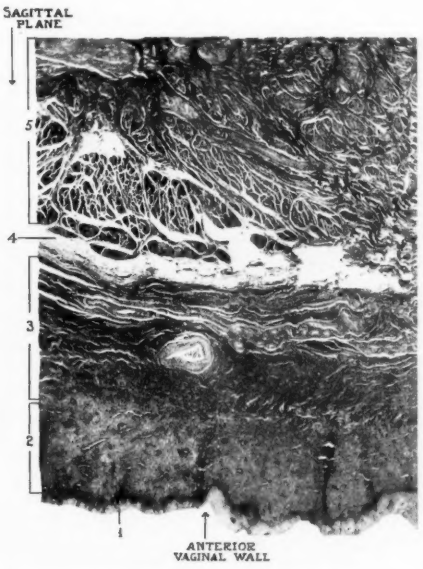


Fig. 10. High power photomicrograph of anterior vaginal wall and adjoining bladder wall from cross section *D*. *1*, Stratified squamous epithelium of vaginal mucosa; *2*, fibro-elastic tunica propria of vaginal mucosa; *3*, muscular coat of vaginal wall; *4*, vesicovaginal layer of areolar fascia; *5*, muscular coat of bladder wall.

fibers sectioned in different planes. Above the muscular coat is the mucosa of the vesical trigone which is composed of transitional epithelium and a loosely arranged fibro-elastic tunica propria. It is to be noted that in this section the muscular coat of the anterior vaginal wall and the muscular coat of the bladder wall do not fuse as did the muscular coat of the vaginal wall and the muscular coat of the urethral wall in the two preceding sections, A and B, but that the muscular coat of the vaginal wall and the muscular coat of the bladder wall are distinctly separated by a thin layer of areolar connective tissue to which the term areolar fascia can logically be applied, since this loosely arranged fibrous tissue is composed of the fibers and cells essential to the structure of a fascia. The application of the term fascia to this tissue is in accord with the definition followed throughout the present study.

Section D (low power photomicrograph, Fig. 9, and high power photomicrograph, Fig. 10) is a section through the upper portion of the anterior vaginal wall and the adjoining wall of the bladder just below the cervicovesical junction. An examination of the section from below upward shows the mucosa of the anterior vaginal wall which is composed of a layer of stratified squamous epithelium and a fibro-elastic tunica propria. Above the mucosa is the muscular coat of the vaginal wall, and above that there is a thin layer of fascia of the areolar type. Above this fascia is the muscular coat of the bladder wall, and above the muscular coat is the mucosa which is composed of a tunica propria and the characteristic transitional epithelium. In this section, as in all of the preceding ones, there is no tissue either in the vaginal wall or the bladder wall which is termed fascia by histologists.

Section E (low power photomicrograph, Fig. 11, and high power photomicrograph, Fig. 12) is an oblique section through the posterior vaginal wall, the anterior rectal wall as

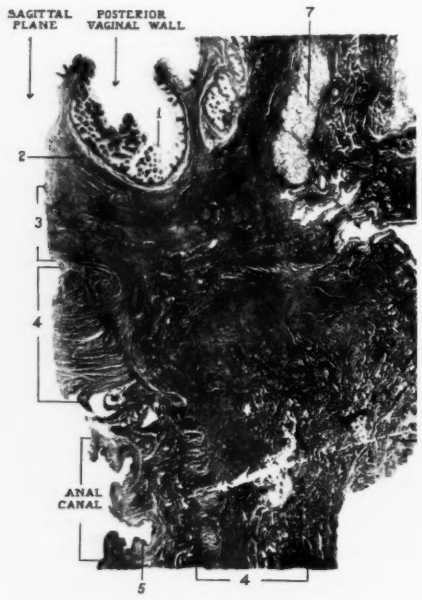


Fig. 11. Low power photomicrograph of section *E* which passes obliquely through the posterior vaginal wall, the muscular coat of the anterior rectal wall, and the wall of the anal canal at a level just above the point where the vagina attaches to the superior layer of the triangular ligament. *1*, Stratified squamous epithelium of vaginal mucosa; *2*, fibro-elastic tunica propria of vaginal mucosa; *3*, muscular coat of vaginal wall; *4*, muscular coat of rectal wall and wall of anal canal; *5*, mucosa of anal canal; *6*, part of levator ani muscle; *7*, vulvovaginal gland.

Fig. 12. High power photomicrograph of posterior vaginal wall, the muscular coat of the anterior rectal wall, and the wall of the anal canal from section *E*. *1*, Stratified squamous epithelium of vaginal mucosa; *2*, fibro-elastic tunica propria of vaginal mucosa; *3*, muscular coat of vaginal wall; *4*, muscular coat of anterior rectal wall and wall of anal canal; *5*, vulvovaginal gland.

it turns backward to become the anal canal, and the wall of the anal canal. An examination of the section from above downward shows the mucosa of the posterior vaginal wall which is composed of a layer of stratified squamous epithelium and a fibro-elastic tunica propria. Beneath the vaginal mucosa is the muscular coat of the vaginal wall fusing with the musculature of the rectal and anal walls. Beneath the smooth muscle of these walls is the submucosa and the mucosa of the anal canal. There is no fascia between the vaginal wall and the wall of the anal canal.

Section F (low power photomicrograph, Fig. 13, and high power photomicrograph, Fig. 14) is a cross section through the posterior vaginal wall and the rectal wall at a point midway between the upper and lower extremities of the vagina. An examination of the section from above downward reveals the mucosa of the posterior vaginal wall which is composed of a layer of stratified squamous epithelium and its tunica propria. Beneath the mucosa is the muscular coat of the posterior vaginal wall. Separating the muscular coat of the vagina from the muscular coat of the rectal wall is a layer of fascia which is of the areolar type in places and of a denser type in others as it passes laterally toward the levator ani muscle and backward to surround the rectal wall. In its denser portion it contains some smooth muscle fibers which run into it from the muscular coat of the vaginal wall. Below the muscular coat of the rectal wall is the submucosa and the rectal mucosa. At the right side of the section part of the levator ani muscle can be seen. Its superior surface is covered by a layer of dense fascia—the superior

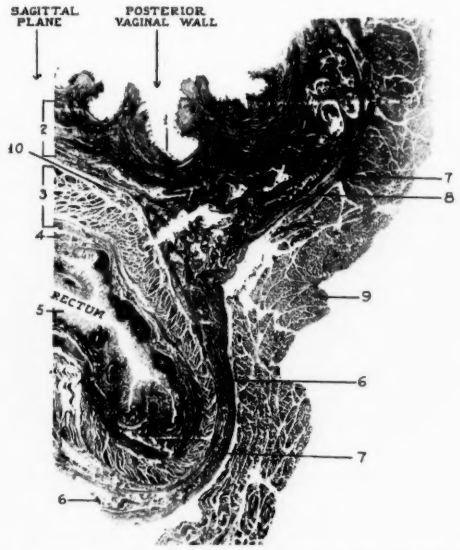


Fig. 13. Low power photomicrograph of cross section *F* which passes through the posterior vaginal wall and the rectal wall at the midpoint of the posterior vaginal wall. *1*, Stratified squamous epithelium of vaginal mucosa; *2*, muscular coat of vaginal wall; *3*, muscular coat of rectal wall; *4*, submucous coat of rectal wall; *5*, rectal mucosa; *6*, rectal layer of the fascia endopelvina; *7*, superior fascia of pelvic diaphragm (superior levator fascia); *8*, lateral portion of the perivaginal fascia; *9*, levator ani muscle; *10*, rectovaginal layer of areolar fascia.

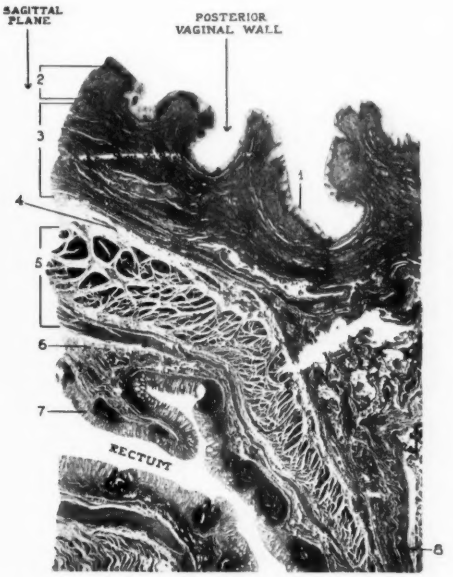


Fig. 14. High power photomicrograph of the posterior vaginal wall and rectal wall from cross section *F*. *1*, Stratified squamous epithelium of vaginal mucosa; *2*, fibroelastic tunica propria of vaginal mucosa; *3*, muscular coat of vaginal wall; *4*, rectovaginal layer of areolar fascia; *5*, muscular coat of rectal wall; *6*, submucous coat of rectal wall; *7*, rectal mucosa; *8*, rectal layer of fascia endopelvina.

fascia of the pelvic diaphragm—which is in contact with the lateral portion of the fascia which surrounds the vagina. Halban has emphasized the fact that the fascia which covers the superior surface of the levator ani muscle does not send layers of fascia inward to surround the pelvic viscera (Fig. 18). It is obvious that this contention is substantiated by conditions in this section. There is in this as in all of the preceding sections no tissue in the wall of the vagina or the wall of the rectum which is termed fascia by histologists. Between the vaginal wall and the rectal wall there is a layer of fascia which in places is of the areolar type and in others of a denser type.

Section G (low power photomicrograph, Fig. 15, and high power photomicrograph, Fig. 16) is a cross section through the posterior lip of the cervix, the upper extremity of the posterior vaginal wall just below the attachment of the vaginal wall to the cervix, and the rectal walls. An examination of the section from above downward reveals a part of the posterior lip of the cervix. Below this is the mucosa of the posterior vaginal wall which is composed of the usual layer of stratified squamous epithelium and a thin tunica propria. Beneath the mucosa is the muscular coat of the vagina which is separated from the muscular coat of the rectal wall by a broad zone of loosely arranged fascia of the areolar type. Beneath this layer of fascia is the muscular coat of the rectal wall with its fibers arranged in an inner circular and an outer longitudinal layer. The muscular coat of the rectal wall is separated from the characteristic rectal mucosa by a thin submucosa. In this section there is no tissue in either the vaginal wall or the rectal wall which is termed fascia by histologists. Between the muscular coat of the vaginal wall and the muscular coat

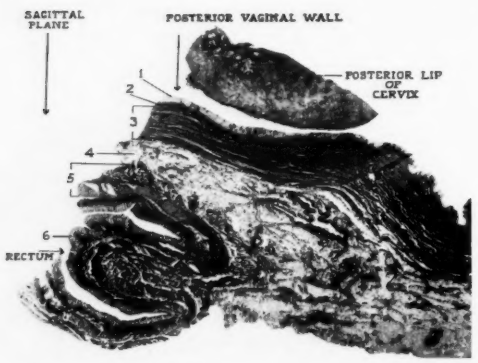


Fig. 15. Low power photomicrograph of cross section *G* which passes through the posterior lip of the cervix, the posterior vaginal wall, and the wall of the rectum just below the cervicovesical junction. *1*, Stratified squamous epithelium of vaginal mucosa; *2*, fibro-elastic tunica propria of vaginal mucosa; *3*, muscular coat of vaginal wall; *4*, rectovaginal layer of areolar fascia; *5*, muscular coat of rectal wall; *6*, rectal mucosa.

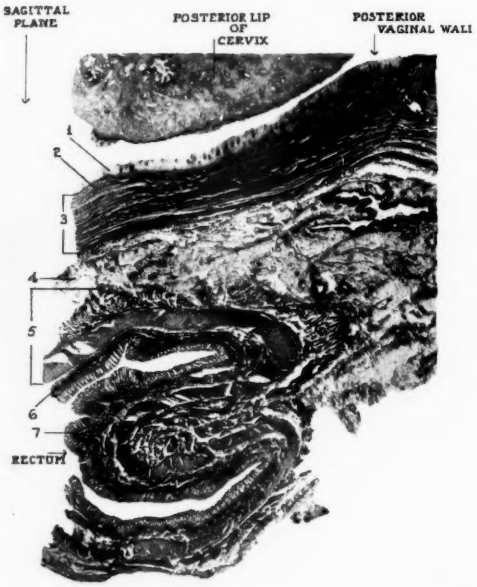


Fig. 16. High power photomicrograph of the posterior vaginal wall and wall of the rectum from cross section *G*. *1*, Stratified squamous epithelium of vaginal mucosa. *2*, fibro-elastic tunica propria of vaginal mucosa; *3*, muscular coat of vaginal wall; *4*, rectovaginal layer of areolar fascia; *5*, muscular coat of rectal wall; *6*, submucous coat of rectal wall; *7*, rectal mucosa.

of the rectal wall there is a broad zone of fascia of the areolar type which extends laterally beneath the vaginal wall as it broadens in the vault.

The findings in the sections described may be briefly summarized by saying that there is no tissue in the walls of the vagina, urethra, bladder, anal canal, and rectum which is termed fascia by histologists. There is no fascia between the vaginal wall and the wall of the urethra. There is, on the contrary, a thin layer of loosely arranged fascia of the areolar type between the anterior vaginal wall and the wall of the bladder, and between the posterior vaginal wall and the wall of the rectum. These two layers of areolar fascia unite at the sides of the vagina to form the perivaginal fascia.

The application of the term fascia to the thin layer of loosely arranged fibro-elastic tissue which separates the vaginal wall from the walls of the bladder and rectum may be challenged. If so, the use of the term may be defended on two grounds: first, this tissue differs from the denser form of connective tissue commonly known as fascia only in the arrangement and number of the white fibers; second, it is continuous with and similar to that important retroperitoneal layer of connective tissue which is found about and between the pelvic viscera, and which is termed fascia endopelvina.

It is desirable at this point to review briefly the gross anatomy of the fascia which surrounds the vagina. For the first lucid description of the fascial system of which the perivaginal fascia is a part and also of the other fascia of the pelvis, credit must be given to Halban who contends that there are two distinct systems of fascia in the pelvis, one which forms sheaths for the voluntary pelvic muscles (muscle fascia) and the other which partly or completely surrounds and separates the pelvic viscera (fascia endopelvina, Fig. 17 and Fig. 18). Halban emphasizes the fact that the endopelvic fascia, though laterally in contact with and loosely attached to the muscle fascia which covers the superior surface of the levator ani muscle (superior fascia of the pelvic diaphragm), is not a part of it.

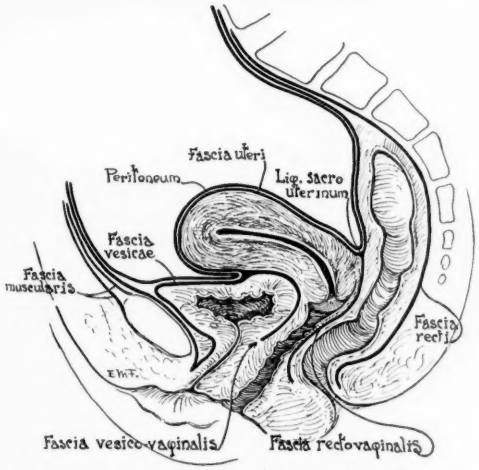


Fig. 17. Sagittal section of pelvis which shows the muscle fascia and the fascia endopelvina. (Modified and redrawn from Halban.)

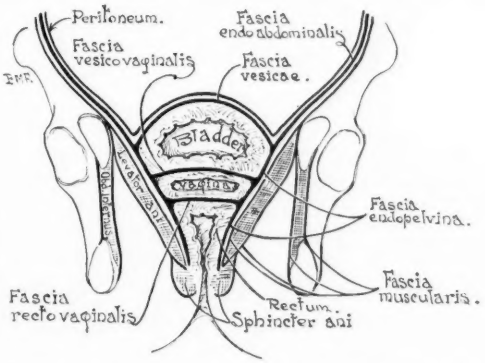


Fig. 18. Frontal section of pelvis which shows the muscle fascia and the fascia endopelvina. (Modified and redrawn from Halban.)

In other words, the fascia which covers the superior surface of the levator muscle does not send layers of fascia inward to surround the pelvic viscera, but continues downward and inward over the surface of the muscle to join the corresponding layer of fascia from the opposite side in a common raphe behind the rectum. According to Halban's description, the perivaginal fascia is a part of the fascia endopelvina.

Halban has also suggested a meaningful terminology for the various layers of the fascia endopelvina. To that layer of areolar fascia which separates the anterior vaginal wall from the adjoining bladder wall the term vesicovaginal fascia is given. To the layer of areolar fascia which separates the posterior vaginal wall from the wall of the rectum the term recto-vaginal fascia is given. The vesicovaginal layer and the rectovaginal layer unite at the sides of the vagina to form the perivaginal fascia, or the perivagina fibrosa, as it is termed by Halban. It is obvious that such terms are indicative of the location of the various layers of this fascia.

Histologists speak of the fibrous coat of the vagina and of the bladder. An examination of the sections herein illustrated shows that the fibrous coats of these structures are but parts of the loosely arranged fascia which separates them. When the histologist separates the bladder wall from the vaginal wall, and examines them separately, he finds a small amount of the fascia adherent to the muscular coat of each. To this thin zone of adherent connective tissue he gives the term fibrous coat.

Finally, in presenting the study herein described, I admit that the findings in a single specimen of any sort do not establish incontrovertible facts. However, taking into consideration that the specimen which has been studied was removed intact from the body of a remarkably well formed and developed young nullipara, and also that the tissues throughout the specimen have conformed closely to the classical descriptions as given by histologists, it is reasonable to believe that the conditions found in this specimen are in all probability indicative of those which exist in the usual normal nullipara.

## CONCLUSIONS

1. In the normal nullipara there is no tissue in the walls of the vagina, urethra, bladder, and rectum which can logically be termed fascia, if the classical histologic descriptions of the tissues are observed.

2. There is no fascia between the anterior vaginal wall and the wall of the urethra.

3. There is a thin layer of fascia of the areolar type between the anterior vaginal

wall and the wall of the bladder. There is a similar layer of areolar fascia between the posterior vaginal wall and the wall of the rectum.

4. The layer of areolar fascia which separates the anterior vaginal wall from the wall of the bladder (vesicovaginal fascia) and the layer of areolar fascia which separates the posterior vaginal wall from the wall of the rectum (rectovaginal fascia) unite at the sides of the vagina to form the perivaginal fascia, which is a part of the fascia endopelvina.

5. The areolar character of the fascia which separates the vaginal wall from the walls of the bladder and rectum makes it impossible to dissect it as an individual layer, and as such to use it in vaginal plastic operative procedures. If used at all, it must be used in conjunction with the overlying wall of the vagina.

6. There is no fascia other than the areolar perivaginal fascia available for use in the surgical correction of cystocele and rectocele.

7. The successful surgical correction of cystocele, rectocele, and urethrocele depends on the utilization of the tissues of the vaginal wall rather than on the use of the fragile areolar fascia which surrounds it.

8. When using the term fascia in descriptions of vaginal plastic operations it is important to stress the fact that the fascia referred to is not of the dense type, such as is the sheath of the rectus muscle, but that it is of the loosely arranged areolar type.

9. It is apparent that many gynecologists have applied the term fascia to the muscular coat of the vaginal wall, which is situated just beneath the vaginal mucosa, because it somewhat resembles a layer of dense fascia in its gross appearance. It is obvious that such use of the term fascia is not in accord with classical histological description of the tissues which constitute the vaginal wall.

10. The abandonment of an inaccurate terminology which is based on the gross appearance of the tissues, and the adoption of one based on the established histology of the tissues in and about the walls of the vagina, urethra, bladder, and rectum, will lead to a clearer common understanding of the problems of cystocele, rectocele, and urethrocele, and will facilitate the teaching of vaginal plastic surgery.

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# GRAVES' CONSTITUTION (WARTHIN)

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THE modern surgical treatment of Graves' disease has its scientific foundation in the thyreogenic theory of Moebius, that a pathological secretion of the thyroid gland is the underlying factor. It is generally accepted that the therapeutic success depends on the removal of a portion of the diseased organ, large enough to inhibit the increased or perverted secretion.

In a very interesting paper, Warthin comes to the opposite view: that thyroid hypersecretion is not the primary pathogenic factor in this disease, but that the thyroid gland is only one of many other organs, secondarily involved in a constitutional abnormality. By analyzing a material of 976 resected thyroid glands, he demonstrated, in 401 specimens obtained from cases which were clinically diagnosed as exophthalmic goiter or toxic adenoma, as the only constant histological feature the presence of hyperplastic lymph follicles, not only in the glands with epithelial hyperplasia, but also in 93 cases in which the latter was completely absent.

From a further study of 1,000 thyroid glands at autopsy he found that all cases with lymphoid hyperplasia in the thyroid gland (94) and 35 additional cases of exophthalmic goiter were associated with the general picture of the thymicolymphatic constitution. Warthin considers, therefore, the presence of lymph follicles in the thyroid gland as evidence of a status thymicolymphaticus which is the underlying factor of every case of Graves' disease and so-called toxic adenoma. An adenoma of the thyroid, in his opinion, is clinically important, as far as so-called toxic symptoms are concerned, only when it is associated with this diathesis. He comes to the practical conclusion that there is, of course, no cure for any primary constitutional defect by operation, as the stigmata of the latter will persist.

Simpson studied a material of 665 resected thyroid glands and found that of these, 265 exophthalmic goiters and 121 adenomatous colloid goiters with toxic symptoms showed only one constant histological finding—lymphoid hyperplasia in the thyroid gland, whereas epithelial hyperplasia was absent in 95 specimens. Of 265 autopsies, 47 cases presented the evidence of thymicolymphatic constitution and in all but 2 the thyroid gland was rich on lymphoid tissue. Simpson agrees, therefore, with Warthin, that all cases of Graves' disease and so-called toxic adenoma possess an identical underlying constitutional abnormality,—the thymicolymphatic diathesis; that these individuals are consequently predestined from birth to hyperthyroidism, and that the disturbance in the morphology and function of the thyroid gland is but one manifestation of an abnormality involving many other structures, which is called "Graves' constitution (Warthin)."

Groups of lymphocytes in the thyroid gland were described as an important feature of the exophthalmic goiter by the earliest students of this disease—Askanazy, Farner, F. Mueller. McCallum was the first who called attention to lymph follicles with germinal centers as typical findings in exophthalmic goiter. His observations were confirmed later by A. Kocher, Simmonds, v. Werdt, Zander, Oehler, Pettavel, Roussy and Clunet, Vogel, Marine and Lenhart. There was, however, no unanimity of opinion in regard to the frequency of lymphoid hyperplasia in exophthalmic goiter. A. Kocher and Simmonds predicated the occurrence of lymphoid hyperplasia in about 80 per cent, Troell in 90 per cent, while v. Werdt found it only in one-half of his typical cases, and much less in his atypical cases. In the latter, Simmonds observed groups of lymphocytes in only 16 per cent. In Wegelin's material of exophthalmic goiter, 91 per cent presented lymphoid tissue the incidence and amount of which were in direct proportion to the epithelial hyperplasia and in inverse proportion to the amount of colloid.

Extensive studies by Simmonds have further shown that lymphocytes may be

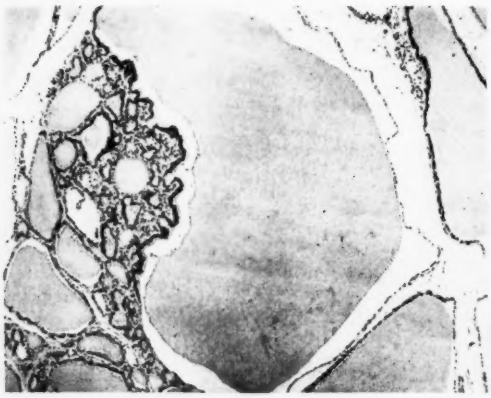

Fig. 1. Non-proliferant diffuse colloid goiter. The projections of the acinar wall indicate that the diffuse colloid goiter is not due to simple pressure distention of normal acini by colloid, but to an active hyperplastic process.

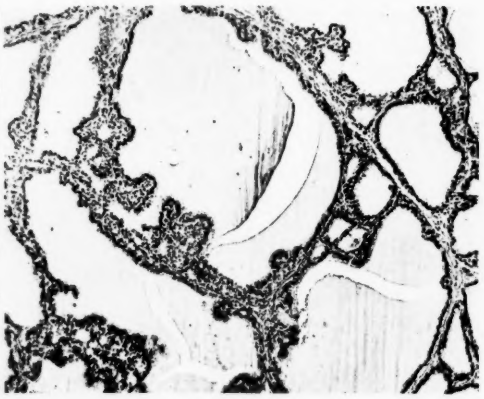

Fig. 2. Proliferant diffuse colloid goiter. Marked epithelial hyperplasia in the large acini. This specimen was taken from a case of severe hyperthyroidism (without exophthalmos).

present even in the normal thyroid gland. As a rule, they were small and oval or round in form; in addition to lymphocytes, plasma cells were present and in one-third of the positive cases, Simmonds described typical lymph follicles with germinal centers. As to the frequency of these changes, Simmonds saw lymphoid tissue in 5 per cent of normal thyroid glands, mostly after the sixtieth year of life, whereas the first two decades were almost free. The female sex predominated and constituted about four-fifths of all his positive cases. The theory advanced by v. Gierke and Borchardt that this lymphoid tissue in the thyroid gland is a manifestation of status thymicolymphaticus was opposed by Simmonds, v. Werdt, and Wegelin because they were unable to find such manifestation in the thyroid glands of typical cases suffering from this constitutional defect, and practically never in childhood, the favorite age for this abnormality.

As the lymphoid tissue is rather frequent in thyroids of older women who are anæmic and adipose, Hacker was of the opinion that there might be some relation to the function of the ovaries. Wegelin, on the other hand, considers the adrenals responsible in some cases, as he saw lymphocytes in the thyroid gland of patients with Addison's disease.

Langhans, Zuellig, Zehbe, Hedinger, and others described groups of lymphocytes in malignant goiter and Hashimoto, Bruenger, Reist, and v. Werdt in cases of chronic thyroiditis.

From all these different observations Wegelin comes to the conclusion that lymphoid tissue develops in the thyroid gland as a purely local response to chemical, mechanical, or bacterial irritation and that there is not any positive proof that it is due to a thymicolymphatic constitution.

The object of our study was to determine whether Warthin's and Simpson's observations could be confirmed by our own findings. The material examined consisted of 53 thyroid glands removed at St. Francis Hospital by operation, and of 7 thyroid glands obtained at autopsy.

The clinical and microscopic diagnoses of our operative material are tabulated in Table I, in which Aschoff's classification is followed. Of our 15 diffuse colloid goiters 8 belonged to the simple and 7 to the proliferative form. Both groups had large acini, filled with well stained colloid, but in the proliferative form the epithelial wall of the follicles showed more foldings and cushion-like elevations, the lumina appeared irregular, and beneath the epithelial lining of the projections many very small acini were formed. This proliferant colloid goiter showed transitions to the exophthalmic goiter by still higher proliferations of

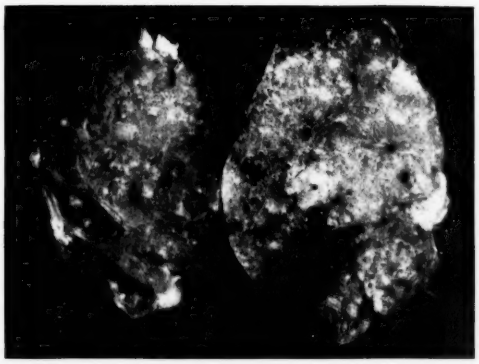

Fig. 3. "Primary" exophthalmic goiter. Small areas of epithelial hyperplasia in a diffuse colloid goiter.

the acinar wall, whereby the lumina became narrow, branching ducts.

Marine and Lenhart attempted to differentiate primary and secondary exophthalmic goiter, the first originating in a normal, the other in a goitrous gland. The expediency of this division seems questionable. From my own studies, not alone of this material, but also of many glands from patients of European extraction, I am forced to the belief that exophthalmic goiter develops usually in a diffuse colloid goiter. All of the thirteen exophthalmic goiters examined in this paper presented on the cut surface either throughout or in patches an amber red and translucent appearance suggesting a colloid rich tissue. Histologically in every instance, areas with large colloid-filled acini were present, either with or without proliferation of the acinar wall. That these changes are not due to an involution caused by Plummer's treatment is indicated by the fact that I saw them also in European material and in exophthalmic goiters obtained from Dr. Hertzler's clinic which were resected prior to the era of pre-operative lugolization.

Marine's statement that every diffuse colloid goiter develops from epithelial hyperplasia of the thyroid gland by involution, should be replaced by the conception that diffuse colloid goiter and exophthalmic goiter are two nearly related stages of thyroid activity and that one of them can easily change into the other.

Fig. 4. Nodular hyperplasia (Wegelin), representing a transitional stage between diffuse and nodular colloid goiter. Clinically a mild hyperthyroidism was present.

Epidemiological statistics are in favor of this opinion, since diffuse colloid goiter, with or without hyperthyroidism, is commonly associated in the same locality with Graves' disease; but there is little statistical evidence in regard to its association with congenital goiter and cretinism. In more mountainous countries the thyreotoxic goiter is an exception and the nearer one approaches the center of the endemic area, the less he meets with

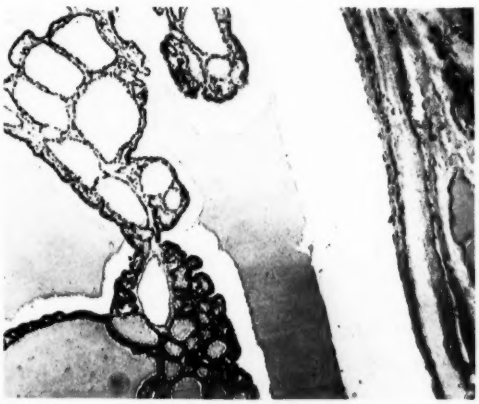

Fig. 5. Nodular colloid goiter. The epithelial proliferations in the nodule are not in favor of Rienhoff's theory that these colloid nodules are merely sequels to accumulation of colloid and involution of the gland.

Fig. 6, left. Diffuse colloid goiter without proliferation. Clinical diagnosis: toxic adenoma.

Fig. 7. Nodular colloid goiter with hyperthyroidism. This case was diagnosed clinically as "toxic adenoma." By palpation, this form of goiter cannot be differentiated from the diffuse colloid goiter shown in Figure 6. The clinical symptoms of both cases were identical.

colloid goiter. It is replaced by the colloid poor, diffuse parenchymatous goiter in childhood and by the adenomatous parenchymatous goiter, the so-called fetal adenoma, in adults.

Two of our operative cases were listed as nodular hyperplasia (Wegelin), which condition is termed by Goetsch diffuse adenomatosis. Even by microscopic examination this type cannot be diagnosed as nodular or diffuse colloid goiter and apparently represents a transitional stage between both.

So-called fetal adenoma was found five times among 53 resected glands. Since Michaud and Hitzig have disproved the theory of Woelfler who regarded it as originating from interacinar embryonic cell rests, the misnomer "fetal adenoma" should be eliminated from the terminology and replaced by the term "nodular parenchymatous goiter." This structure is the most frequent type of goiter encountered in the center of severe endemic districts. In Bern, Switzerland, for instance, Woelz found this form in 76 per cent of the surgical goiter material, and Wydler reported it in 91 per cent of cretins, who represent the severest manifestation of endemic goiter. In countries with a very mild incidence of goiter, on the other hand, the parenchymatous nodular goiter is so infrequent that Hertzler is inclined to separate it completely from the common goiter and proposes for it the term "mixed tumor." This view is limited to a single goiter region, where colloid and exophthalmic goiters are the two most frequent structures, and, in my opinion, is no more justifiable than the opposite conception of some authors who, living in a severe endemic area, regard exophthalmic goiter as a disease without any relation to simple goiter. That the nodular parenchymatous goiter does not represent an entity of thyroid disease, independent of other forms of goiter, is further proved by the fact, that not seldom parenchymatous and colloid structures are associated in the same gland and even in the same nodule. This combination was noticed three times in our material.

Of our 10 nodular colloid goiters 7 were grouped according to Aschoff as non-proliferant and 3 as proliferant forms. Regarding

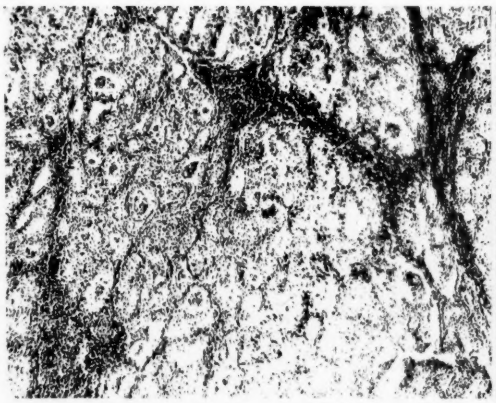

Fig. 8. Lymphoid tissue in exophthalmic goiter. No typical lymph follicles were found.

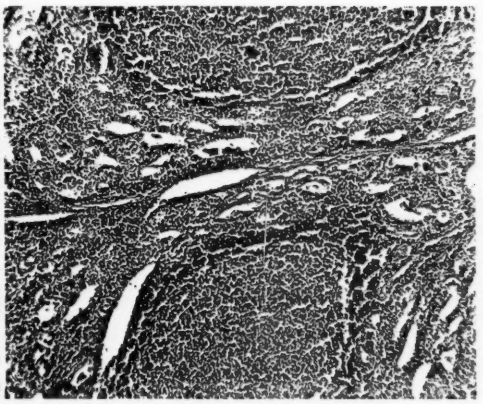

Fig. 9. Lymph follicles with germinal centers in a diffuse microfollicular goiter without any thyreotoxic symptoms.

the histogenesis of the colloid nodules, we may say that our experience does not confirm the view held by Rienhoff that these structures are merely regressive sequelæ of a previous diffuse hyperplasia, due to pressure distention of acini with colloid. We believe that these nodules originate, like the diffuse colloid goiters, as a proliferative process from a pre-existing thyroid pattern. We have to regard, therefore, the terms "non-proliferative" and "proliferative" colloid goiter only as different grades of the same pathological process, and we must use great care in drawing conclusions concerning the function of a nodular gland, since it seems almost impossible in a specimen with many, sometimes over a hundred nodules, to get a correct impression of the histological character of the whole gland, by examining sections from only a few different areas.

Of our 51 benign goiter cases, 14 were clinically diagnosed as exophthalmic goiter and 22 as toxic adenomata. Only 10 of the latter showed nodules anatomically, the other 12 were diffuse colloid goiters. From this it is apparent that the clinical diagnosis "toxic adenoma" does not refer to the anatomical structure at all, but only to the absence of eye symptoms in the patient. It would be logical to omit, therefore, this misleading name and designate these cases with a purely clinical diagnosis: "hyperthyroidism without eye signs." The diagnosis of exophthalmic goiter was made by the clinician 14 times, and of these the anatomical examination revealed in 2 cases diffuse colloid goiter without epithelial proliferation; in 4, proliferant colloid goiter; and in 8, exophthalmic goiter, which showed islands of solid epithelial hyperplasia within a diffuse colloid goiter. No adenomatous gland was found in this group. Protrusion of the eyes was absent in 5 of the 13 patients, whose thyroid glands were typical exophthalmic goiters. We regard, therefore, exophthalmic and so-called toxic goiter as different stages of the same pathological entity, i.e., hyperthyroidism. In Table I three grades of hyperthyroidism are distinguished: XXX: severe hyperthyroidism with exophthalmos; XX: severe hyperthyroidism without exophthalmos; X: mild hyperthyroidism; *: goiter without hyperthyroidism.

In the group of nodular colloid goiter, no case belonged to the severest form of hyperthyroidism, 1 to the second grade, and 5 to the mild grade of hyperthyroidism. In our material, parenchymatous nodular goiter (fetal adenoma) never produced thyreotoxicosis, with the exception of one case. In this the clinician had diagnosed toxic adenoma, but the enucleation of the single adenoma did not bring any relief from the toxic symptoms, and the basal metabolism was still 25 per cent

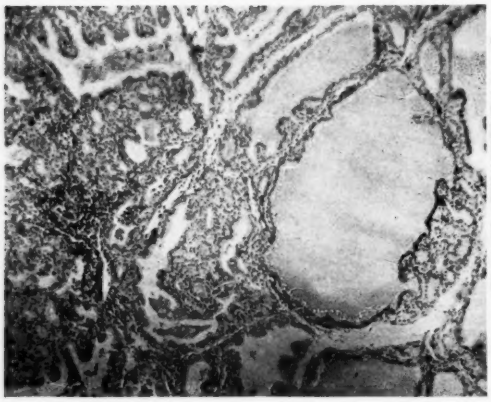

Fig. 10. Exophthalmic goiter, originating in diffuse colloid goiter. The lymphocytic infiltration is limited to the hyperplastic cellular area.

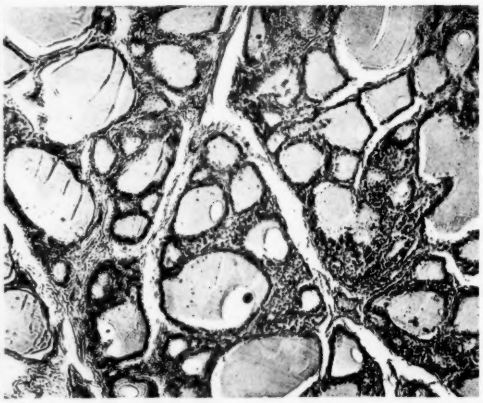

Fig. 11. Thyroid gland of a typical case of status thymicolymphaticus. There is no lymphoid tissue in the thyroid gland.

above normal, 1 year after the operation. We assume that in this case hyperplastic changes in the non-resected thyroid tissue proper were responsible for the clinical symptoms, a point brought out recently in a valuable study by Rienhoff.

In Table III are tabulated the findings showing the relation of lymphoid tissue to the epithelial structure of the gland and in Table IV the same to the clinical diagnosis. All but one of our typical exophthalmic goiters with marked epithelial hyperplasia showed lymphoid tissue. It was found either in the crossings of the interlobular septa, or invading the periphery of the lobules, the acini being compressed. In 5 of these specimens there were rather small and infrequent groups of lymphocytes with some plasma cells, in 7 their size was considerable, and in 3 of the 13 cases, typical lymph follicles with germinal center were present, including reticulum cells and lymphoblasts. The only case in which the most careful search failed to detect lymphoid tissue was a 29 year old man with a severe form of Graves' disease of 5 months' duration. The basal metabolism was 72 per cent above normal and dropped after iodine administration to 17 per cent. The gland was a diffuse colloid goiter with many islands of dense epithelial hyperplasia. Groups of lymphocytes were present in 71.3 per cent of the proliferative diffuse colloid goiters and in 1 we found typical lymph follicles; of the non-proliferant forms of diffuse colloid goiter only one-third had positive findings; none of these glands showed typical lymph follicles.

In the 2 cases of nodular hyperplasia (Wegelin) and in 5 of the 10 nodular colloid goiters we were unable to detect any lymphoid infiltration. In the 5 positive cases the lymphoid tissue was only scanty and never within the nodules, but only in the surrounding parenchyma proper, which was compressed by the growing colloid nodules. One of the parenchymatous nodular goiters showed small groups of lymphocytes, near the capsule of an adenoma.

From Table IV we learn the most important relationship between the frequency of lymphoid tissue and the clinical diagnosis. Comparing our findings with those of Warthin and Simpson, we were surprised that of our 14 cases of Graves' disease only 71.4 per cent had lymphoid tissue in their thyroid gland, although we examined many sections from different parts of the resected gland. The second group in Table IV includes our severe grades of hyperthyroidism without eye signs, and the microscopic examination revealed lymphocytes in 69 per cent; in the third group of mild hyperthyroidism, only 55 per cent had positive findings. Still more surprising were our findings in the cases of goiter without thyreotoxic symptoms. Of these

TABLE I.—ANATOMICAL DIAGNOSIS, AGE, AND GRADE OF HYPERTHYROIDISM

Simple diffuse colloid goiter

| Sex | Age | Grade |
|---|---|---|
| Female | 19 | * |
| Male | 27 | xx |
| Female | 41 | xx |
| Female | 25 | xxx |
| Female | 21 | xx |
| Female | 41 | xxx |
| Female | 26 | * |
| Female | 23 | x |

Proliferant diffuse colloid goiter

| Sex | Age | Grade |
|---|---|---|
| Female | 19 | xx |
| Female | 23 | xxx |
| Male | 46 | xx |
| Male | 40 | x |
| Male | 29 | xxx |
| Female | 24 | xxx |
| Male | 24 | xxx |

Exophthalmic goiter

| Sex | Age | Grade |
|---|---|---|
| Female | 26 | xxx |
| Female | 28 | xx |
| Female | 32 | xx |
| Female | 24 | xxx |
| Female | 21 | xxx |
| Female | 34 | xx |
| Male | 29 | xxx |
| Female | 32 | xx |
| Female | 20 | xxx |
| Male | 48 | xxx |
| Female | 27 | xxx |
| Female | 42 | xxx |
| Female | 42 | xx |

Nodular hyperplasia (Wegelin)

| Sex | Age | Grade |
|---|---|---|
| Female | 38 | x |
| Female | 36 | x |

Nodular colloid goiter without proliferation

| Sex | Age | Grade |
|---|---|---|
| Female | 49 | x |
| Female | 52 | x |
| Male | 38 | * |
| Female | 39 | * |
| Female | 55 | x |
| Male | 42 | * |
| Female | 18 | * |

Nodular colloid goiter with proliferation

| Sex | Age | Grade |
|---|---|---|
| Male | 37 | xx |
| Female | 25 | x |
| Female | 50 | x |

Nodular parenchymal goiter

| Sex | Age | Grade |
|---|---|---|
| Female | 40 | * |
| Male | 44 | * |
| Male | 30 | * |
| Female | 30 | * |
| Female | 40 | x(?) |

Nodular colloid and parenchymal goiter

| Sex | Age | Grade |
|---|---|---|
| Male | 29 | xx |
| Female | 30 | * |
| Male | 33 | * |

xxx Severe hyperthyroidism with exophthalmos.
xx Severe hyperthyroidism without exophthalmos.
x Mild hyperthyroidism.
* No hyperthyroidism.

fully 38.5 per cent showed lymphocytic infiltration, and the greatest degree of lymphoid hyperplasia, which was observed in any of our cases, was noted in group 4. A married woman, 30 years old, who had treated the enlargement of her neck with large doses of iodine for one whole year, had a normal basal metabolism and no other signs of hyperthyroidism. After resection of 45 grams of thyroid a marked postoperative myxœdema developed, which today, 3 years after operation, still needs thyroid medication. Histologically the resected gland showed small acini with low epithelium and viscous colloid, and an enormous hyperplasia of lymph follicles. The microscopic picture corresponded to Hertzler's description of his "interstitial goiter."

The second largest amount of lymphoid tissue was seen in the adenocarcinoma of a 61 year old woman, who died of multiple metastases one year after thyroidectomy was performed.

TABLE II.—PATHOLOGICAL AND ANATOMICAL DIAGNOSIS, AGE, AND SEX OF OUR GOITER CASES

| Diagnosis | Age in years and sex | | | | |
|---|---|---|---|---|---|
| | 12–15 | 16–19 | 20–25 | 26–45 | 46–60 |
| Small follicular hyperplasia | .... | .... | ..... | 1F | ..... |
| Diffuse colloid goiter without proliferation | .... | 1F | 4F | 1M 2F | ..... |
| Diffuse colloid goiter with proliferation | .... | 1F | 1M 2F | 2M | 1M |
| Exophthalmic goiter | .... | .... | 3F | 1M 8F | 1M |
| Nodular hyperplasia (Wegelin) | .... | .... | ..... | 2F | ..... |
| Nodular colloid goiter without proliferation | .... | 1F | ..... | 2M 1F | 3F |
| Nodular colloid goiter with epithelial proliferation | .... | .... | 1F | 1M | 1F |
| Nodular parenchymatous goiter | .... | .... | ..... | 2M 3F | ..... |
| Nodular colloid and parenchymatous goiter | .... | .... | ..... | 2M 1F | ..... |

TABLE III.—RELATIONSHIP OF LYMPHOID TISSUE IN THYROID GLAND AND ANATOMICAL DIAGNOSIS

| | Cases |
|---|---|
| Simple diffuse colloid goiter | |
| Much lymphoid tissue | 1 |
| Some lymphoid tissue | 1 |
| Scanty lymphoid tissue | 1 |
| No lymphoid tissue | 5 |
| Proliferant diffuse colloid goiter | |
| Much lymphoid tissue | 2 |
| Scanty lymphoid tissue | 3 |
| No lymphoid tissue | 2 |
| Exophthalmic goiter | |
| Very much lymphoid tissue | 2 |
| Much lymphoid tissue | 3 |
| Some lymphoid tissue | 4 |
| Scanty lymphoid tissue | 3 |
| No lymphoid tissue | 1 |
| Nodular hyperplasia (Wegelin) | |
| No lymphoid tissue | 2 |
| Nodular colloid goiter without proliferation | |
| Some lymphoid tissue | 3 |
| Scanty lymphoid tissue | 1 |
| No lymphoid tissue | 3 |
| Nodular colloid goiter with proliferation | |
| Scanty lymphoid tissue | 1 |
| No lymphoid tissue | 2 |
| Nodular parenchymal goiter | |
| Scanty lymphoid tissue | 1 |
| No lymphoid tissue | 4 |
| Nodular colloid and parenchymal goiter | |
| Scanty lymphoid tissue | 1 |
| No lymphoid tissue | 2 |

TABLE IV.—RELATIONSHIP OF LYMPHOID TISSUE IN THYROID GLAND AND CLINICAL DIAGNOSIS

| | Cases |
|---|---|
| Severe hyperthyroidism with exophthalmos | |
| Very much lymphoid tissue | 2 |
| Much lymphoid tissue | 2 |
| Some lymphoid tissue | 3 |
| Scanty lymphoid tissue | 3 |
| No lymphoid tissue | 4 |
| Percentage of positive findings, 71.4 | |
| Severe hyperthyroidism without exophthalmos | |
| Much lymphoid tissue | 5 |
| Some lymphoid tissue | 3 |
| Scanty lymphoid tissue | 1 |
| No lymphoid tissue | 4 |
| Percentage of positive findings, 69 | |
| Mild hyperthyroidism | |
| Some lymphoid tissue | 2 |
| Scanty lymphoid tissue | 3 |
| No lymphoid tissue | 4 |
| Percentage of positive findings, 55 | |
| Goiter without hyperthyroidism | |
| Very much lymphoid tissue | 1 |
| Some lymphoid tissue | 1 |
| Scanty lymphoid tissue | 3 |
| No lymphoid tissue | 8 |
| Percentage of positive findings, 38.5 | |

### RESULTS OF OUR STUDY

Our findings corroborate the conclusions drawn by European workers, that the lymphocytic infiltration in exophthalmic goiter is due to the pathological hyperplasia and hypersecretion of the thyroid itself. Without doubting their diagnostic value, we must keep in mind the fact that only 66 per cent of all our thyreotoxic cases presented lymphocytic groups in the thyroid gland and that, on the other hand, more than one-third of the innocent goiters without clinical signs of secretory disturbance showed the same findings. From Table III it is evident that the frequency and size of the lymphocyte groups depend directly on the intensity of the hyperplasia and the decrease of the stored colloid. By studying exophthalmic goiters, in which the epithelial hyperplasia does not affect the whole gland but develops in patches within a diffuse colloid goiter, it is easy to recognize that the lymphocytes collect only in or around the cellular hyperplastic islands, and that the colloid-rich areas are practically free from round cells. This is certainly not in favor of Warthin's theory that the lymphoid tissue is a manifestation of a constitutional abnormality, because in this case we would expect it evenly distributed over the whole gland, independent of the epithelial hyperplasia. Another proof that the lymphocytic infiltration is due to the proliferation of the acinar cells and to the pathological secretion of the exophthalmic goiter itself, is the influence of iodine treatment on the morphology of hyperplastic goiter. Rienhoff was the first who pointed out that the lymphoid hyperplasia was much less pronounced after iodine administration as compared with cases in which Lugol's solution had not been given. In a recent paper, I reported that in 30 cases of Graves' disease in which iodine was not given, 2 glands were without any groups of lymphocytes, 5 had a few, and 23 had many groups. In 30 other exophthalmic goiters removed after iodine medication, I found

that lymphocytic infiltration was absent in 10 glands, scanty in 7, abundant in 13. This shows that the lymphoid tissue decreases as the hyperplasia and hypersecretion of the thyroid gland is inhibited by iodine.

Warthin's contention that a status thymicolymphaticus is associated always with lymph follicles in the thyroid gland is not substantiated by the observations of Simmonds, v. Werdt, and Wegelin. In our own material there were 2 cases of sudden death, which presented all anatomical signs of a thymicolymphatic constitution, but failed to show any lymphoid tissue in their thyroid glands.

## CONCLUSIONS

1. Warthin's and Simpson's theory that in Graves' disease the thyroid gland is not the chief pathogenic factor, but an incidental complication and sequela to a constitutional anomaly, is not confirmed by our study.

2. The most important histological criterion of Graves' disease, as far as the thyroid itself is concerned, is not the presence of hyperplastic lymph follicles throughout this gland.

3. Of our cases of Graves' disease and toxic goiter only 66 per cent had lymphoid tissue in the thyroid gland, and of the cases without clinical symptoms of thyreotoxicosis 38.5 per cent showed lymphocytic infiltration.

4. In our typical cases of status thymicolymphaticus, the thyroid gland was free from lymphocytes.

5. Lymphocytic infiltration of the thyroid is not a manifestation of an underlying constitutional anomaly, but is a purely local response to hyperplasia and hypersecretion of the gland.

6. Our findings are in complete agreement with the theory of Moebius that hypersecretion of the thyroid gland is the essential cause of Graves' disease.

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# CORPUS LUTEUM OF PREGNANCY[1]

## Persistence of Pregnancy after Excision of the Corpus Luteum in the Early Weeks

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THE function of the corpus luteum of pregnancy in relationship to an existing pregnancy has been the subject of much discussion and theorizing. I wish to report observations made upon three cases in which the corpus luteum of pregnancy was excised. In one of these, the existing pregnancy was not disturbed and persisted approximately to the fifth month. Physiological ablation experiments in the human naturally are not common and instances in the literature of operative removal of the corpus luteum of pregnancy or of its destruction are rare enough to be worthy of consideration. The early work of Beard, Prenant, and Born suggested that the existence of pregnancy in the uterus depended upon the corpus luteum and its secretions. Fraenkel produced abortion in pregnant animals by destroying corpora lutea with a cautery. Loeb showed in guinea pigs that, for the production of traumatic deciduomata, i.e., the sensitization of the uterus, essential for the formation of deciduomata which is itself essentially the reaction of maternal placenta formation, the corpus luteum was necessary. Frank states that the removal of corpus luteum at operation is often followed by premature menstruation, when the pregravid activation of the mucosa has already taken place and that during pregnancy, the corpus luteum inhibits follicular ripening as well as the cyclic engorgement of the genitals which might disturb the developing ovum. He also holds that any foreign body may stimulate the endometrium sensitized by corpus luteum to form the maternal portion of the placenta (Loeb). According to Frank, the corpus luteum of pregnancy is essential to the life of pregnancy at most only in the first 6 weeks. The placenta, i.e., previously fetal trophoblast, presumably elaborates an identical or similar hormone which suffices then for the continued existence of the pregnancy. De Lee disturbed, at laparotomy, corpora lutea of pregnancy, in two cases. He reimplanted the corpus luteum material in the broad ligaments as free grafts in each case. An abortion occurred at 4 weeks and 1 week, respectively.

We excised the corpus luteum of pregnancy under a variety of circumstances in the following cases:

Case 1. K. S., white, aged 29 years, ii-para. Case No. 18593. Patient entered the Lakeside Hospital June 5, 1928, complaining of intermittent bleeding occurring May 3, 1928, lasting one and one-half days, and associated with severe pain in the lower abdomen. Three weeks later the pain again became severe and patient was admitted to the hospital after 4 days during which she had passed a few small clots of blood. The last menstrual period began April 8, 1928; previous menstrual period had begun March 15, 1928, and was normal in character. Patient has two children aged 6 and 4 years and had one spontaneous abortion 3 years ago at 3 months. The anamnesis was negative otherwise. Physical examination revealed a well developed and quite well nourished young woman, afebrile, fairly comfortable. The general physical examination was negative. Vaginal examination revealed a marital outlet and the cervix transversely lacerated, particularly on the left. It was dilated admitting freely the tip of the index finger, and there were large blood clots in the vagina and protruding from the cervix. The uterus was enlarged approximately to the size of a 6 weeks' pregnancy, and was quite hard and smooth in outline. The amount of bleeding, the wide dilatation of the cervix and the consistency of the uterus made the diagnosis of inevitable abortion seem obvious. On June 6, 1928, the uterus was curetted bluntly. Old black blood clots were removed together with a small piece of placental tissue approximately the size of the end of one's index finger. The uterus had the consistency of involution, being quite firm although definitely enlarged. The uterus was swabbed with tincture of iodine and the tip of an iodoform gauze drain was left in the uterine cavity.

*Pathological report.* The histological sections showed normal placental tissue. Approximately 4 weeks later, July 6, the patient was readmitted to the hospital with the complaint of pain in the right lower quadrant. For 2 weeks she had been bleeding intermittently. On examination the outlet was marital, the cervix hard and firm, the uterus anterior, the size of a small orange and of very firm consistency. There were no lateral palpable masses. It seemed likely the subinvolution and bleeding

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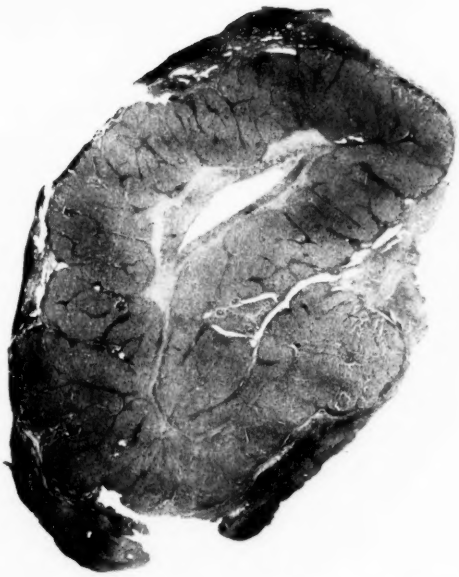

Fig. 1. The fairly large corpus luteum of pregnancy which was removed from the left ovary of Case 1. There is characteristic development of lutein cells about the central cavity.

Fig. 2. Fragment of corpus luteum of pregnancy removed from Case 3. There is the small development of paralutein cells which is characteristic of the first half of pregnancy.

might be due to a piece of retained placenta. It failed to occur to me that this patient could have become pregnant again. The patient elected to have tubal sterilization in addition, inasmuch as she was to have a general anæsthetic, and this request was granted.

At operation on July 7, 1928, the uterus was found to be globular and quite firm, the cervix was easily dilated, and a fairly profuse flow of blood followed dilatation. The uterine cavity seemed hollow and empty when a curette was passed into it. Curettings were small in amount. The uterine cavity was swabbed with iodine and a small pack was inserted which was removed in 24 hours. The abdomen was opened through a low midline incision and the uterus was found to be enlarged and slightly softer than normal. The color did not suggest pregnancy, the uterus being normally pale. Resection of the cornual portion of the tubes was done. The uterine cornua were closed and the proximal ends of the distal fragment of tubes were buried in the broad ligaments. The uterine portions of the tubes were completely excised and the uterine musculature closed firmly with interrupted sutures. The patient previously had had an appendectomy. There were no other abnormalities in the abdomen.

There was found a fairly large corpus luteum in the left ovary (Fig. 1) which was shelled out gently and the ovarian defect closed with fine interrupted sutures. The right ovary was normal. The corpus luteum measured about 1 centimeter in diameter. Histologically, the corpus luteum (Fig. 4) revealed vascularization and no degenerative changes. Curettings were moderate in amount and showed large decidual cells, some of which were in good condition and some of which showed degeneration with large engorged venous sinuses. Examination a few weeks later showed no reduction in the size of the uterus. In September, a roentgenogram showed the evidence of fetal bones. About September the patient began to pass pinkish, thin fluid from the uterus. This stopped and the uterus increased in size normally until November 11, 1928, when the patient passed a thin serosanguineous pinkish fluid and the following day she began to have labor pains and suddenly ruptured the membranes prolapsing the umbilical cord. The cervix was found to be dilated a finger's breadth, and as the fetus was dead she was allowed to continue in labor and was delivered of a dead fetus of approximately 5 months the following evening, the placenta which was normal being expelled spontaneously. Grossly, the fetus was normal. The patient's convalescence was uneventful.

The failure of this pregnancy to be disturbed by chemical and surgical traumata in the form of iodine application and curetting,

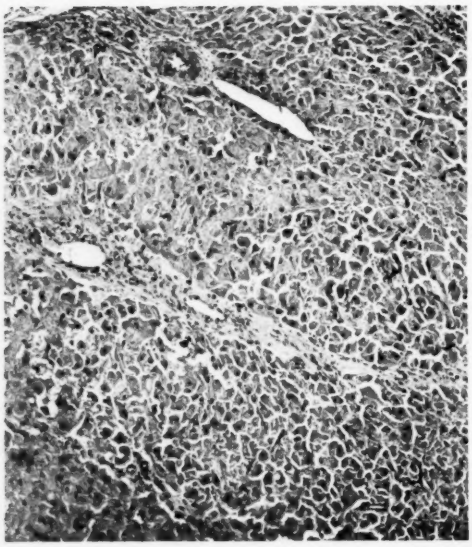

Fig. 3. High power view of corpus luteum of pregnancy from Case 2. There is a well marked connective tissue stroma.

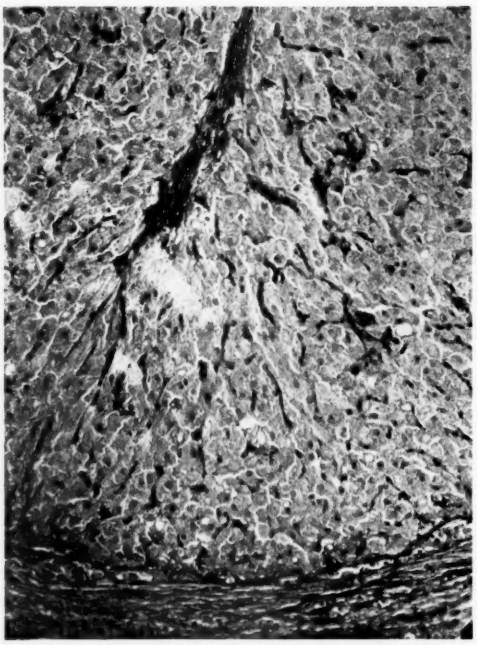

Fig. 4. The section shows a high power view of corpus luteum of pregnancy near the periphery showing stroma and small groups of paralutein cells. There are visible many of the colloid bodies pathognomonic of corpus luteum of pregnancy (Marcotty).

seems almost impossible although the possibility of this pregnancy being in a rudimentary horn of a bicornuate uterus which would offer it some protection, must be kept in mind. This consideration and the size of the fetus in November seemed to suggest that the corpus luteum was excised when the maximum duration of the pregnancy could not exceed 4 weeks.

CASE 2. L. S., aged 33 years, ii-para. Case No. 115925. This was a patient of Dr. Elliott C. Cutler. She was admitted to the Lakeside Hospital complaining of abdominal distention and obstipation. She was 3½ months pregnant. Physical examination was negative except for a distended abdomen with no tenderness, rigidity, or visible peristalsis. Clinical and X-ray studies confirmed the diagnosis of megacolon, and cæcostomy was planned as a preliminary step. Laparotomy was done with the plan of performing an ileosigmoidostomy. The uterus was soft, injected, and appeared to be about 4 months pregnant. Anastomosis was performed between ileum and sigmoid.

There was a rather large, well preserved corpus luteum of the right ovary which was excised, it having been planned previously to terminate the pregnancy at another procedure. One month later, the patient, who was making a perfectly normal and satisfactory convalescence and was up and about, developed distention and following effective catharsis by castor oil, the cæcostomy wound began to herniate and became constricted and finally gangrenous. Hyperpyrexia and high leucocytosis 19,000 followed, and the patient, at this point, developed a show of blood and went into labor with regular pains and miscarried spontaneously. The onset of labor here probably was due to the peritonitis.

CASE 3. H. D., aged 30 years. Case No. 11920. Patient was a white, married woman of 30 years complaining of persistent vomiting, hyperemesis gravidarum, amenorrhœa, and a sensation of prolapse. An unilateral oophorectomy had been done 5 years ago for ovarian cyst, and a therapeutic abortion in 1927 for pernicious vomiting of pregnancy. The menstrual periods had been regular the last period occurring February 18, 1929. Sterilization had been recommended for this patient at the time of the therapeutic abortion. On examination, the outlet was found to be rather markedly relaxed, the cervix normal, the uterus anterior freely movable and apparently normal in size and consistency. There were no lateral masses. On March 14, 1929, a dilatation and curettage was done and a rather thick endometrium was removed. There was nothing to indicate pregnancy. A low midlin

incision was made in the abdomen and the pelvis was inspected. The uterus seemed to be very slightly enlarged. There was an early corpus luteum of pregnancy of the left ovary. The right ovary was missing. One centimeter of tube was excised from the cornua on either side and the raw areas peritonized with the round ligament. The corpus luteum was excised (Fig. 2).

*Pathological examination.* The corpus luteum revealed large, thick zone of lutein cells surrounding a central lumen containing coagulated blood about the periphery. A small zone of the cortical portion of the ovary was seen. Sections of uterine scrapings presented an intact hyperplastic surface epithelium, the glands exhibiting marked hypertrophy and hyperplasia with budding. They were dilated and tortuous. The stroma contained congested vascular channels with areas of early decidua, but no chorionic villi were found. The diagnosis of corpus luteum of pregnancy and uterine pregnancy was made.

## SUMMARY AND CONCLUSIONS

Scrutiny of the history of Case 1 suggests the occurrence of preliminary pregnancy beginning after the menstrual period of April 8, 1928. At the beginning of May, bleeding occurred and 3 weeks succeeding, May 29, 1928, the patient had a spontaneous abortion. At that time the uterus was approximately the size of a 6 weeks' pregnancy and on curettage a piece of placenta about 1 by 2 centimeters was recovered. Inasmuch as the uterine cavity was swabbed out with iodine, it seems reasonable to suppose that this pregnancy was definitely interrupted. About 5 weeks later, the patient was readmitted to the hospital complaining of intermittent bleeding for 2 weeks and the uterus was slightly enlarged. The curettings showed large decidual cells. The corpus luteum of pregnancy was excised at this time, which was probably not in excess of 5 weeks' duration. The previous curettage and miscarriage confused the picture somewhat but it seems scarcely reasonable to believe that any pregnancy less than 2 months would survive the curettage with the removal of a fairly large section of the placenta, the swabbing of the uterus with iodine and subsequent packing with gauze. Here, then, in all probability, we have a pregnancy progressing to its second half without corpus luteum of pregnancy from what may reasonably be assumed to be a duration of about 4 or at most 5 weeks. Essen-Moeller reports a case of bilateral oophorectomy in which it appeared that the corpus luteum may have been excised within the first month of pregnancy. This pregnancy had proceeded to term.

In Case 2 we have the corpus luteum of pregnancy excised at the fourth month. This was followed by an abortion. However, the administration of cathartics and later the presence of peritonitis is more than sufficient cause to induce uterine cramps and abortion so no conclusion can be drawn.

The corpus luteum was removed in Case 3 incidentally for histological examination when the tubal sterilization was performed. This patient had not missed a period but thought she was pregnant, she having developed nausea. The evidence offered by Case 1 allows one to state with some assurance, that in the human, pregnancy is independent of the hormone supplied by the corpus luteum of pregnancy once its duration exceeds approximately 4 to 6 weeks.

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# A HORMONE TEST FOR THE DIAGNOSIS OF EARLY PREGNANCY

## Clinical Application in 100 Cases, Preliminary Report

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THE diagnosis of early pregnancy, and its differentiation from other pelvic conditions, can at present be accomplished with a considerable degree of accuracy by means of the Aschheim-Zondek test. This test is based on the fact, first, that large amounts of the hormone of the anterior pituitary body are excreted in the urine during pregnancy, and, second, that when urine containing this hormone is injected into immature mice, ovulation occurs.

As outlined by Aschheim, the procedure necessitates the use of five or six immature female mice, 3 weeks of age, for each experiment. Varying quantities of urine are injected into each mouse, three times daily, over a period of 2 days. Autopsy is done one hundred hours after the first injection, and the presence of ovulation as demonstrated by the macroscopic and microscopic presence of corpora lutea and corpora hæmorrhagica, give positive evidence of pregnancy in the patient from whom the urine was obtained. In a report of one thousand cases, Aschheim demonstrated 98.2 per cent accuracy, and stated that in the cases in which accurate results were not obtained in the first test, subsequent tests gave results which were later substantiated.

Friedman (3), in his work on ovulation in the rabbit, demonstrated that intravenous injection of 5 cubic centimeters of urine from a pregnant woman provokes ovulation in the same manner as in the mouse, the advantage being that ovulation occurs within 24 hours, either because of the injection of a single large amount directly into the blood stream, or because of the sexual peculiarities of the rabbit. Friedman injected eighteen rabbits with urine from pregnant women and obtained positive results in each instance. Fourteen rabbits, each injected with urine from non-pregnant women, all gave negative results. This work increased the value of the test by materially decreasing the time element, simplifying the technique, and apparently maintaining as great a degree of accuracy as that obtained by Aschheim and Zondek.

Friedman's results were so striking that it was decided to use the test in a series of cases in an attempt to determine its clinical value as a practical procedure in the diagnosis and differential diagnosis of *early* pregnancy.

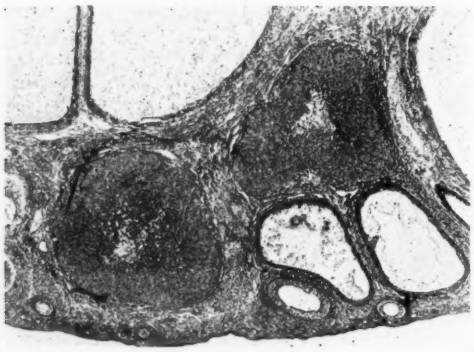


Fig. 1. High-power photomicrograph of portion of rabbit ovary, after injection of urine from pregnant patient, 12 days after opening of tubes by inflation with carbon dioxide, showing two well developed corpora lutea. ×40.

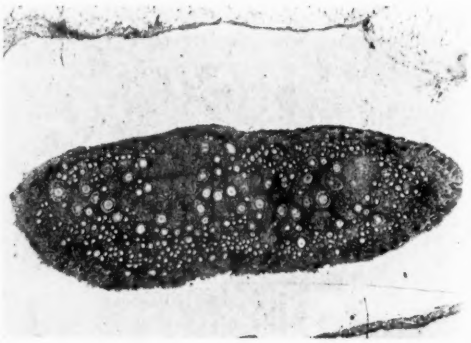
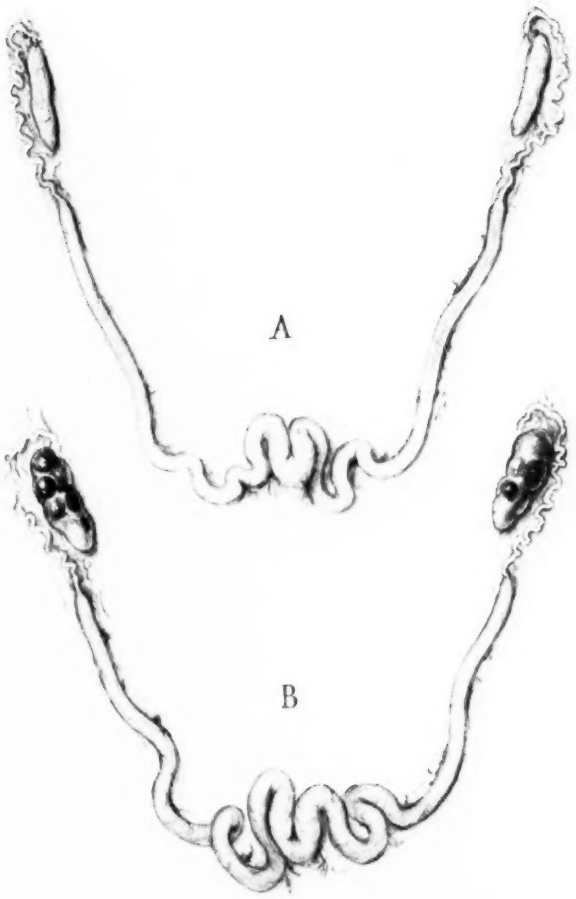


Fig. 2. Low-power photomicrograph of rabbit ovary after injection of urine from non-pregnant patient, showing no corpora lutea or corpora hæmorrhagica. ×25.




A. Bicornate uterus, tubes, and ovaries of a 14 week rabbit, 30 hours after injection of 7 cubic centimeters of urine from a non-pregnant patient. This demonstrates a negative result, with no changes occurring in the ovaries.

B. Bicornate uterus, tubes, and ovaries of a 14 week rabbit, 30 hours after injection of 7 cubic centimeters of urine from a pregnant patient. This demonstrates a positive result from an approximate 5 weeks' pregnancy, showing the presence of numerous corpora lutea and corpora hemorrhagica.

*Plate I. A Hormone Test for the Diagnosis of Early Pregnancy.—P. F. Schneider.*

UNIV. OF MICH.

Enumeration of the factors involved in this test will in a measure explain the technique which has been developed. The rabbit does not as a rule copulate or go into heat until the age of 5 months during the summer, and 6 to 8 months during the winter (Hammond and Marshall). The rabbit has no regular cycle, does not ovulate unless it copulates, and following copulation, ovulation occurs in 8 to 10 hours (Friedman, 4). By using rabbits not over 12 to 14 weeks of age, the possibility of ovulation from other causes than the injection of the hormone is reduced to a minimum. We have found that when rabbits under 3 months of age are used, the results are not constant and are of little value.

It has been demonstrated that the blood stream of many individuals at times contains the hormone of the anterior pituitary body, but that during pregnancy the amount is increased so greatly that it is excreted in the urine. It has been demonstrated that the ovarian hormone also is excreted at times in varying amounts in the urine of women (Loewe and Lange). This follicular hormone (Frank) causes uterine hypertrophy but does not cause ovulation. Animal experimentation with fresh pituitary substance has established the pituitary hormone as the activating factor which is the cause of ovulation in the tests described (Friedman).

The occurrence of ovulation in the rabbit is demonstrated by the macroscopic presence of corpora hæmorrhagica and corpora lutea at autopsy and can be further established by microscopic examination. Friedman has found the free ova present in the fallopian tube following this test.

### TECHNIQUE IN PRESENT SERIES

The technique requires the use of one female rabbit 12 to 14 weeks of age. A specimen of the first urine voided in the morning is obtained in a clean receptacle. From 5 to 7 cubic centimeters of this urine is injected into the marginal ear vein. Sterile precautions are not necessary in making the intravenous injection. Mortality among the rabbits has been a negligible factor, and can be almost entirely eliminated by using only clear specimens, the urine being filtered if cloudy. Autopsy is done in from 24 to 30 hours after injection, and an immediate diagnosis is possible by macroscopic inspection of the ovaries. If negative, the ovaries remain small in size and show no change. If positive, from one to fourteen corpora hæmorrhagica and corpora lutea are found present in each ovary. In some instances, a positive result has been obtained in 12 hours, and it has become our custom to inject two rabbits in cases in which a diagnosis of pregnancy might influence a decision regarding operation. The first rabbit is then autopsied at 12 hours, and the result can be checked by autopsy on the second rabbit at 24 or 30 hours without loss of time.

### TYPES OF CASES STUDIED

We have used the test in a series of one hundred cases which are divided into three groups: (1) 25 positive control cases in which a diagnosis of pregnancy was previously established by other means; (2) 25 negative control cases in which it was definitely known that there could be no pregnancy present; and (3) 50 test cases in which pregnancy was suspected but could not be diagnosed.

*Positive control cases.* The approximate stage of the pregnancies in the 25 positive control cases was:

| | Cases |
|---|---|
| 3d month | 5 |
| 4th month | 1 |
| 5th month | 4 |
| 6th month | 1 |
| 7th month | 5 |
| 8th month | 4 |
| Term | 5 |

In each of these a positive result was obtained and the diagnosis of pregnancy checked by subsequent clinical findings.

*Negative control cases.* The 25 negative control cases were:

| | Cases |
|---|---|
| Normal | 2 |
| Male | 3 |
| Menopause | 3 |
| Complete ovariectomy | 1 |
| Complete ovariectomy with carcinoma | 1 |
| Postpartum | 15 |

In this series of non-pregnant cases, all results were negative with the exception of 5 in the postpartum series. The postpartum cases were tested to determine how long the positive reaction persists after delivery.

*Postpartum cases.* In the 15 postpartum cases, the urine, obtained at varying intervals after delivery, was tested with the following results:

| Cases | Interval postpartum | Result |
|---|---|---|
| 1 | 12 hours | positive |
| 2 | 18 hours | positive |
| 2 | 24 hours | positive |
| 1 | 24 hours | negative |
| 1 | 26 hours | negative |
| 1 | 41 hours | positive |
| 1 | 67 hours | positive |
| 2 | 4th day | negative |
| 2 | 7th day | negative |
| 2 | 10th day | negative |

It is seen that the reaction disappears very rapidly following delivery, and that it was found absent in one instance 24 hours, and in another 26 hours after delivery. In two other cases a positive reaction was obtained 41 and 67 hours post delivery.

*Test cases.* In this series of cases, in which pregnancy was suspected but could not be diagnosed, 20 gave positive results by the test and in each instance were confirmed by subsequent events. The 30 others gave negative results and, in all except two instances, subsequent events proved the test to be correct. In these two instances negative results were obtained at first, but later tests proved positive. These inaccuracies occurred when, for the first time, 6 week rabbits were used. Subsequent tests with 12 week rabbits gave positive results which later were proved to be correct. This demonstrated that it is impossible to obtain accurate results if the rabbits are not sufficiently mature.

### ABBREVIATED REPORTS OF ILLUSTRATIVE CASES

CASE 6. Mrs. M. The tubes were found closed February 13 by tubal inflation, with no penetration of carbon dioxide. Inflation was repeated February 20, and after using pressure up to 210 millimeters, the mercury column suddenly dropped with entrance of gas into the peritoneal cavity. Twelve days following the last tubal inflation, 6 cubic centimeters of urine injected into a rabbit yielded a positive result in 24 hours. The accompanying photomicrograph (Fig. 2) of the ovary of the test rabbit shows the presence of the corpora lutea and corpora hæmorrhagica, and subsequent events demonstrated the presence of a normal pregnancy in the patient.

CASE 49. Mrs. H. Last pregnancy terminated February 17, 1930. Normal menstrual periods recurred April 8 and May 12. On June 9 patient gave a history of being nauseated by cigarette smoke, a symptom which was present early in the previous pregnancy. Menses were due June 12 to 16. Test from specimen obtained June 10 gave a positive result. Menses had not occurred July 1.

CASE 50. Mrs. F., aged 38 years. Patient had had one criminal abortion 10 years ago, and had subsequently been sterile. Inflation of tubes March 6, 1930, showed obstruction with apparent failure of gas to pass through the tubes. Inflation was repeated March 13, 1930, with apparently negative results. Last menstrual period was May 3. On May 29, iodized oil was injected into the uterus, and the X-ray showed the tubes to be patent, the oil passing into the peritoneal cavity. The menstrual period which should have occurred May 31 did not appear, and a test from specimen obtained June 5 gave a negative result. Patient stated that if pregnancy were present, it must have occurred prior to May 29, and probable date was May 21 or May 26. The test was repeated with a specimen obtained June 10 and gave a strong positive reaction.

CASE 4. Mrs. J., iv-para. The menses which were always regular, of 30 day type, had been delayed 3 days. Previous menstrual period was normal. A third degree retroversion was present. Five cubic centimeters of urine was injected into a rabbit. The test gave a positive result. Subsequent events demonstrated the presence of a normal pregnancy.

CASE 5. Mrs. S., ii-para. Patient gave a history of incomplete abortion with constant bleeding from December 10 to January 9. No subsequent menstrual periods occurred in February. She had a third degree retroversion. Seven cubic centimeters of urine were injected into a rabbit February 13 and gave a positive result. Examination at a later date verified the diagnosis of pregnancy.

CASE 10. Mrs. P., iv-para. No menstrual period had occurred since termination of last pregnancy, September, 1929. February 3, 1930, examination revealed the uterus slightly increased in size. Seven cubic centimeters of urine injected into a rabbit gave a positive result. There have been no subsequent menses, and examination on July 3 revealed a 6 months' pregnancy.

CASE 15. Mrs. S., ii-para. Menses had been delayed 10 days. Test positive. Two weeks later patient was sent to hospital with severe uterine bleeding. Test was repeated 2 weeks following cessation of bleeding and gave negative result. Regular menses have appeared.

CASE 28. Mrs. D. Patient gave a history of irregular menses. Last menstrual period was January 9. March 22 physical examination revealed no definite evidence of pregnancy. Test at this time gave positive result. Two weeks later patient was admitted to hospital with intestinal obstruction. Immediate operation followed, with separation of

bands of adhesions about the hepatic flexure of the colon. Cæcostomy was done. Inspection of uterus revealed the presence of a 2 months' pregnancy, and right ovarian cyst, which was removed at this time. Two weeks following operation the test was repeated to determine if it would give any information as to whether the fetus was alive or dead, as patient had had nothing by mouth, and fluids intravenously and subcutaneously only, since operation. Prior to the time of obtaining specimen, there had been no vaginal bleeding, and no evidence that death of fetus had occurred. The test gave a positive result. Forty-eight hours later patient began having uterine contractions and expelled a macerated fetus of from 2 to 2½ months.

CASE 38. Mrs. M. A cystic ovary had been removed 4 years ago. Menses have been regular since that time. She has had amenorrhœa for past 2 months. Examination revealed a third degree retroversion and the presence of a mass which was suspected of being a cystic ovary. Test at this time gave positive result. Forty-eight hours later, patient began having active uterine bleeding, and evacuation of the contents of the uterus revealed a 2 months' pregnancy. A laparotomy showed a large cystic ovary.

CASE 8. Mrs. N. Menses have always been regular. Present menstrual period was delayed 3 days. Test was negative. A normal menstrual period occurred several days later.

CASE 23. Mrs. H. Menses have been irregular. Amenorrhœa had been present for past 2 months. Basal metabolism test indicated the presence of hypothyroidism. Test was negative.

CASE 26. Mrs. E. Last previous pregnancy had been terminated 3 months ago. No menstrual periods had occurred since that time. Pelvic examination revealed a mass in the pelvis the size and consistency of a 2 months' pregnancy. Test was negative. Abdominal operation revealed the presence of a right interligamentous cyst.

CASE 29. Mrs. S. Last pregnancy was terminated in November, 1929. April 12, 1930, there had been no return of the menstrual period. Test was negative. Normal menstrual period occurred May 1, 1930.

CASE 35. Mrs. C. Last pregnancy terminated January, 1930. Patient had had 13 pregnancies during the past 12 years, with only four living children. This condition was accompanied by a chronic nephritis, and sterilization had been advised. A test was carried out to establish definitely the absence of pregnancy prior to operation. A negative result was obtained.

CASE 36. Miss A. Patient gave a history of irregular menstruation. Amenorrhœa had been present for 2 months. Test was carried out to exclude pregnancy as cause of amenorrhœa. Test was negative. Normal menses occurred several weeks later.

CASE 37. Mrs. M. Previous pregnancy was terminated in December. Menses recurred in April. In May the patient presented herself, with a history of the menses being 7 days overdue. The test was negative.

### RESULTS OF STUDY

In the 25 positive control cases in which previous diagnosis of pregnancy was possible, a positive result was obtained by the hormone test in each instance, while in the negative control cases, 25 specimens from non-pregnant patients all gave negative results except as explained previously. This is of significance because it demonstrates that urine from normal non-pregnant women, males, women following menopause, artificial menopause as a result of ovariectomy, or carcinoma, does not give a positive result when tested by the method described. Fluhman, using blood serum instead of urine, obtained positive results in mice in conditions other than pregnancy, as menopause, artificial menopause, functional amenorrhœa, and irregular menstruation. It is known that carcinoma, menopause, and ovariectomy cause a hypertrophy of the pituitary gland, but according to the results reported by Aschheim and Zondek in their work with mice, and the small number of such cases in this series, there is no evidence that the resulting hypertrophy and excretion of the hormone is sufficient to cause a positive result when the urine is used for the test.

The negative control series also brings out the rather significant fact that the hormone quickly disappears from the urine after delivery. The question arises as to whether, in the two cases in which it was positive at 41 and 67 hours after delivery, this delayed disappearance of the reaction was due to retained fragments of placental tissue. Aschheim and Zondek report positive results for their test in only two conditions other than pregnancy, hydatidiform mole, and chorio epithelioma. We have not had either of these conditions available for the present series, but the indications are that the reaction is caused by the presence of embryonic tissue in contact with the maternal tissues, and that it continues as long as this contact is maintained.

The series of test cases from which the case reports have been selected shows that the test is positive very early in the pregnancy, but it has been rather difficult to ascertain how

promptly after the particular intercourse responsible for the pregnancy a positive reaction may be obtained. The suggestion of an answer to this question was obtained in the first 3 cases reported.

In Case 6, it seems likely that the pregnancy occurred following the last tubal inflation, or at the very earliest, following the first inflation, which indicates that a positive result was obtained from 12 to 20 days following the first intercourse at which pregnancy was possible.

In Case 49, a positive result was obtained within 2 to 4 days prior to the date at which the normal menstrual period was expected, the last menstrual period having been normal.

In Case 50, it is likely that the pregnancy occurred as a result of coitus on May 21 or 26, which would mean that a positive test was obtained in approximately 20 days. In this case, the negative result obtained 5 days earlier may be interpreted as indicating the approximate time after which the reaction becomes positive.

This interpretation in the three instances mentioned, leads us to assume that the hormone of the anterior pituitary appears in the urine in sufficient quantity to give a positive test as early as 12 to 20 days following the coitus which is responsible for the pregnancy. Further investigation is necessary to establish this point definitely.

Of equal importance to the positive results obtained in early pregnancy are the negative results in instances of menstrual irregularity in non-pregnant women, demonstrated by amenorrhœa of a duration of from several days to several months. The application of the test where menses have not recurred following a recent pregnancy, and where other symptoms or findings lead to a suspicion of another pregnancy, has given definite results both positive and negative, which have been substantiated in each instance by subsequent events.

## SUMMARY AND CONCLUSION

The small series of cases here presented is inadequate for the purpose of drawing definite conclusions, but may serve as a basis for future work in determining the limitations of the test. Emphasis of the following points seems justified:

1. The simplicity and accuracy of the test indicate that it has a practical value as a diagnostic measure, which is greatly enhanced by the fact that the entire procedure can be completed within 24 hours.

2. Experience with this series of cases indicates that future refinement of the technique will make it possible to decrease the time necessary for the completion of the test to 8 to 12 hours.

3. Application of the test has shown its value effectively in the immediate differentiation of early pregnancy from such conditions as menstrual irregularity due to other causes, delayed return of menses following pregnancy, and pelvic masses simulating pregnancy. Formerly this differentiation required days or sometimes weeks.

4. Application of the test in excluding early pregnancy prior to uterine instrumentation, as in tubal inflation, injection of iodized oil, or pelvic operative work and abdominal surgery or therapeutic use of radium or X-ray should eliminate many of the unfortunate experiences which occur.

5. The rapid disappearance of the hormone after delivery, and the persistence of the reaction following incomplete abortion or death of the fetus, indicate that future investigation may prove the test of value in the diagnosis of retained decidual tissue following labor or incomplete abortion.

6. The question of the diagnosis of ectopic pregnancy, hydatidiform mole, and chorio epithelioma has not been encountered in this series, but provides considerable latitude for future investigation.

I wish to acknowledge the assistance rendered by Dr. W. W. Brandes of the department of pathology of Northwestern University, in the pathological work which was done to confirm the gross findings of the test.

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# THE CAUSE OF DEATH IN LIVER AUTOLYSIS

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IN 1924 our attention was called by the studies of Mason to the extreme toxic reaction produced by implanting pieces of fresh liver in the peritoneal cavity of dogs. One of us extended these observations to other regions of the body showing that similar toxicity was produced if the transplanted liver was introduced into the pleura or subcutaneously. Ellis and Dragstedt more recently have shown that these results were due to the fact that a severe peritonitis was set up due to a bacillus similar to the bacillus welchii organism. In their experiments they show that pieces of autoclaved liver inserted into a dog's abdomen failed to cause peritonitis and also pieces of sterile liver obtained from fetal dogs similarly were non-toxic. The results were therefore attributed to infection arising from bacteria lying latent in the liver. In their review of the literature on the subject they showed that the presence of organisms in the tissues had been recognized for many years and that one observer, Wolbach, had even reported a special anaerobe in dogs' livers.

Our experiments were begun to analyze the mechanism of this peritonitis. The deaths in all the reported series of both ours and those of Mason and Dragstedt were all so prompt (generally within 20 hours) that it seemed inconceivable that a pure infection could be responsible for them. One cannot think of any parallel of the case in which such a small number of organisms introduced intraperitoneally will produce death in from 12 to 18 hours. This is of special significance when one considers the well known immunity of the dog's peritoneum to extraneously introduced infection of any sort. The experimental production of peritonitis has proved in the hands of all observers to be a very difficult matter. Even the complete transsection of the bowel will not in most cases produce such a toxic reaction or prompt death. With these points in view, the following sets of experiments were undertaken.

## EXPERIMENTS

Group I. Two dogs were killed by electrocution. Their livers were removed under aseptic precautions, were cut up and ground with sand in a sterile mortar. The specimens were divided into 100 gram lots and 3 were incubated for 24 hours and 1 for 28 hours. They were then removed from the incubator and autoclaved for 40 minutes under a pressure of 17 pounds. In each case, cultures taken proved them to be sterile after the autoclaving. The 100 gram specimens were then introduced into abdomens of 4 normal dogs and in each case there was prompt death of the animal within 16 hours. Cultures of the peritoneum and transplanted ground liver showed in every case enormous numbers of organisms resembling the bacillus welchii.

The pathological and bacteriological pictures found in the entire series reported in this paper were very much the same and will be described at this point. The organisms were gram positive rods of large size and with thick capsules. Contrary to the experience of Dragstedt and Ellis they caused a strong fermentation of milk in a very high percentage of cases. Of about 100 cultures made there was destructive fermentation of milk with acid formation in all except three strains encountered. This would take place within a 16 to 18 hour period. In the 3 there was a souring of the milk and an acid clot formation. While no further studies have been made as to the bacteriological identification of this organism, we feel justified in assuming that it is simply a strain of bacillus welchii, and it will be referred to as such during the remainder of the paper.

The pathological pictures encountered have also presented a striking similarity. In the vast majority of cases when the intraperitoneal injections or implantations were made in the afternoon, the animal was found dead and cold at 8 o'clock in the morning. In a few cases in which the injections were made in the morning, death occurred before 6 p.m. and occasionally as early as 2 to 3 hours after injection. The findings are all quite typical and are not in the least those of aseptic

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TABLE I.—EFFECT OF PLACING GROUND AUTOLYZED STERILE LIVER INTO THE PERITONEUM

| No. | Material implanted | Culture of implant | Survival hrs. | Culture of peritoneum at autopsy | Postmortem |
|---|---|---|---|---|---|
| 10 | 100 gm. of liver from electrocuted dog removed and ground aseptically incubated 48 hours and autoclaved | Sterile | Less than 18 | B. welchii | Autolytic peritonitis. |
| 11 | Same with 24 hour incubation | Sterile | Less than 18 | B. welchii | Autolytic peritonitis. |
| 12 | Same as No. 11 | Sterile | Less than 24 | B. welchii | Autolytic peritonitis. |
| 13 | Same as No. 12 | Sterile | Less than 16 | B. welchii | Autolytic peritonitis. |

TABLE II.—EFFECT OF PLACING FRESH GROUND STERILE LIVER IN PERITONEUM

| No. | Material implanted | Culture of implant | Survival hrs. | Culture of peritoneum at autopsy | Postmortem |
|---|---|---|---|---|---|
| 22 | 100 gm. of liver from electrocuted dog removed, ground aseptically and autoclaved | Sterile | 72 | Not made | Not typical picture of autolytic peritonitis purulent infection. |
| 23 | Same | Sterile | 40 | B. welchii | Autolytic peritonitis. |
| 24 | Same | Sterile | Killed 17 days | 0 | Material scattered and about half absorbed. |
| 31 | Same | Sterile | Less than 24 | B. welchii | Autolytic peritonitis. |
| 32 | Same | Sterile | Less than 18 | B. welchii | Autolytic peritonitis. |
| 33 | Same | Sterile | Less than 24 | B. welchii | Autolytic peritonitis. |

peritonitis. The abdomen is generally enormously distended with gas if the animal lives more than 12 hours. Upon opening it, there is discovered a large amount of exudate measuring between 300 to 500 cubic centimeters. This exudate contains froth on its surface and bubbles are to be found on the under surface of the liver and the other viscera. It is blood stained and bright red in color. There is generally a comparative absence of deposits of fibrin and in no case have we encountered any frank pus. The entire peritoneal surfaces are intensely inflamed and in most cases there can be seen exceedingly numerous punctate hæmorrhages. These hæmorrhages are not necessarily confined to the peritoneum but occur in the other endothelial surfaces of the body, especially the pleura. There is generally engorgement of the lung and microscopic section showing capillary hæmorrhages in the lung as well. The most striking changes occur, however, in the host's liver. The livers are infiltrated with gas and exceedingly friable and feel greasy to the touch. Microscopic examination reveals an exceedingly advanced stage of liver degeneration with necrotic areas scattered through the tissues and granular cytoplasm about the portal channels, with a minimal infiltration of leucocytes. In other words, we have a picture of a severe toxic reaction and not of a severe infection.

In the series of rabbits, to be reported, the condition was even more striking. Grossly, it was almost impossible to distinguish between the appearance of the transplanted liver and the host's liver. Both showed almost equally severe autolytic changes. On microscopic examination, while the transplanted liver showed more advanced necrosis, the host's liver showed such changes that one could not be sure without reading the labels on the slides which was which. This description will serve for the pathology of all the rest of our report and the picture will henceforth be spoken of as "autolytic peritonitis."

It is evident from these experiments that the livers which have been allowed to autolyze and are then sterilized contain substances which are capable of bringing about this condition of autolytic peritonitis, even in the absence of the bacillus welchii.

Group II. In this set of experiments, normal dogs were electrocuted and 100 gram specimens of their livers taken which were ground and immediately autoclaved (see Table II). They were cultured and shown to be sterile. They were then implanted in

TABLE III.—EFFECT OF VARIOUS FACTORS ON VIRULENCE OF AUTOLYTIC PERITONITIS

| No. | Material implanted | Culture of implant | Survival hrs. | Culture of peritoneum at autopsy | Postmortem |
|---|---|---|---|---|---|
| 46 | 100 gm. fresh ground liver from 14 day bile fistula dog | Sterile | Less than 16 | B. welchii | Autolytic peritonitis. |
| 47 | 100 gm. fresh ground liver from 3 months jaundiced dog | B. welchii | 8–10 | B. welchii | Autolytic peritonitis. |
| Rabbit 1 | 25 gm. solid piece of fresh aseptically removed rabbit liver into upper abdomen | | Less than 16 | B. welchii | Marked autolysis of both transplant and host's liver. No fluid or hæmorrhage in abdomen. Fluid in chest, lungs congested. |
| Rabbit 2 | Same | | 8–9 | B. welchii | Same. |
| Rabbit 3 | Same | | 8–9 | B. welchii | Same. Host's liver incubated 24 hrs. and was riddled with gas. |
| Rabbit 4 | Same | | 8–9 | B. welchii | Same. |
| Rabbit 5 | Same. Same fluid in abdomen | | Killed 10 hrs. | B. welchii, therefore not a postmortem invader | Same, but some fluid in abdomen. Pregnant. |
| Rabbit 6 | Same | | Less than 18 | B. welchii | Same, but no fluid in chest. |
| Dog 4 | 18 c.cm. (2 tubes) of 18 hour milk culture from dog 1 liver. Stormy fermentation | B. welchii | 6 days killed | 0 | Showed no reaction. |

TABLE IV.—EFFECT OF INTRAPERITONEAL INJECTION OF CONCENTRATED STERILE EXTRACT OF AUTOLYZED LIVERS

| No. | Material injected | Culture of material | Survival hrs. | Culture of peritoneum at autopsy | Postmortem |
|---|---|---|---|---|---|
| 25 | 100 gm. ground liver incubated 24 hrs. Boiled 2 hrs. in 1,000 c.cm. water, filtered twice and filtrate boiled down to 25 c.cm. | Sterile | Less than 18 | B. welchii | Autolytic peritonitis. |
| 26 | Same | Sterile | About 12 | B. welchii | Autolytic peritonitis. |
| 18 | Same concentrated to 35 c.cm. | Sterile | 8 | B. welchii | Autolytic peritonitis. |
| 19 | Same as No. 25 | Sterile | 8 | B. welchii | Autolytic peritonitis. |
| 5 | 40 gm. ground liver incubated 24 hrs. Boiled 2 hrs. in 1,000 c.cm. normal salt solution, filtered and boiled down to 35 c.cm. | Sterile | 7–10 | B. welchii | Autolytic peritonitis. |

the upper abdomen through a small buttonhole incision in the midline. Four of the 6 dogs succumbed to an autolytic peritonitis of exactly the same sort as described in Group I. This peritonitis was a little longer in coming on but otherwise presented exactly the same features and in every case large numbers of bacillus welchii were encountered.

It is obvious, therefore, that both in autolyzed and fresh livers, there resides some toxic factor which renders the infection of the implanted material with bacillus welchii a practical certainty. In each case, in both groups of experiments and in many of the subsequent ones, our cultures were watched for a week or more and in no case was there a development of the growth in time such as one might expect from any lurking spores. It is well known of course, as was stated by Ellis and Dragstedt in their paper, that both the bowel and normal tissues contain numbers of bacteria especially of this type. But we have here a mechanism in which by some toxic feature there is a great change in the permeability of the bowel so that they are allowed to pass exceedingly rapidly through the bowel wall and to infect sterile material lying in the peritoneum so as to cause an exceedingly rapid production of a toxæmia of overwhelming virulence.

The seeming variance with these results and those reported by Ellis and Dragstedt is

TABLE V.—EFFECT OF INTRAPERITONEAL INJECTION OF STERILE DILUTE EXTRACT OF AUTOLYZED LIVER

| No. | Material injected | Culture of material | Survival | Culture of peritoneum at autopsy | Postmortem |
|---|---|---|---|---|---|
| 15 | 200 gm. ground liver incubated 24 hrs. extracted 2 hrs. in 1,000 c.cm. boiling water, filtered and boiled down to 400 c.cm. | Sterile | Killed 24 days | Not made | Normal. |
| 16 | 100 gm. ground liver incubated 24 hrs. extracted 2 hours in 1,000 c.cm. boiling water, filtered and boiled to 100 c.cm. | Sterile | 14 days | Not made | Died of distemper. |
| 17 | Same as 16 | Sterile | 24 days | Not made | Normal. |
| 50 | Same as 16 but boiled to 235 c.cm. | Sterile | Killed 5 days | Sterile | Normal. |

TABLE VI.—EFFECT OF INTRAPERITONEAL IMPLANTATION OF PARTIALLY PURIFIED PROTEIN COAGULUM FROM AUTOLYZED LIVERS

| No. | Material implanted | Culture of implanted material | Survival hrs. | Culture of peritoneum at autopsy | Postmortem |
|---|---|---|---|---|---|
| 34 | 100 gm. fresh ground liver autoclaved and extracted 8 hrs. in 4 liters hot water, filtered and precipitate implanted | Sterile | 72 | B. welchii | Autolytic peritonitis. |
| 20 | Same | Sterile | Less than 18 | B. welchii | Autolytic peritonitis. |
| 21 | Same | Sterile | Less than 18 | B. welchii | Autolytic peritonitis. |
| 27 | 100 gm. ground liver incubated 24 hrs. Extracted three times each with 500 c.cm. boiling water, boiling alcohol, boiling ether and alcohol and boiling $CHCl_3$. Remainder dried in water bath, emulsified with 25 c.cm. water | Sterile | Less than 20 | B. welchii | Autolytic peritonitis. |
| 28 | Same | | 23 | B. welchii | Autolytic peritonitis. |

probably due to the fact that while in our experiments the liver was finely ground, in theirs it was implanted in a single large piece. This lump of cooked liver is very hard and does not present anywhere near the surface to expose itself to autolysis as is the case when the liver is ground. The same factor will probably act in the fetal livers in which they reported no disturbance.

Group III. A biliary fistula was established in the normal dog by suture of the bladder to skin in the abdominal wall and the bile was allowed to drain for 14 days. During all this period the animal had acholic stools. He was rapidly losing weight. He was sacrificed and an autoclaved, ground 100 gram specimen of his liver placed within the abdomen of a normal dog. Death resulted in less than 24 hours—the usual picture of autolytic peritonitis.

As a complement to the above experiment, the ground sterilized liver from a dog who had been jaundiced about 3 months was also transplanted into a normal animal and the same picture produced. It was assumed, therefore, that the bile itself or its constituents were probably not vital factors in the process. With this point in view, the Pettenkoffer reacting material in 100 grams of autolyzed liver was determined through the kindness of Dr. Rewbridge, and values of about 0.06 of a gram of bile salts were found. In view of the fact that there certainly were other substances of a Pettenkoffer reacting type in this material in addition to the bile salts, it is quite obvious that this falls far below the lethal dose as was reported by Rewbridge in his work on bile peritonitis. According to his experiments, it took about 2.5 grams of bile salt preparation to produce peritonitis.

The influence of diet was then studied by using herbivorous animals and the liver of one rabbit was planted into 5 other rabbits and exactly the same clinical picture of autolytic peritonitis was produced.

In spite of the well known immunity of the peritoneum to bacterial infection, it was

TABLE VII.—EFFECT OF INTRAPERITONEAL INJECTIONS OF HYDROLYZED EXTRACTS OF AUTOLYZED LIVER

| No. | Material injected | Culture of material | Survival | Culture of peritoneum at autopsy | Postmortem |
|---|---|---|---|---|---|
| 36 | 100 gm. liver ground, incubated 24 hrs. extracted with 4,000 c.cm. material (boiled 2 hrs.) extract boiled 1 hr. with few drops 25 per cent KOH and boiled down to 50 c.cm. | Sterile | Killed 7 days | | Normal. |
| 37 | Same | Sterile | Killed 7 days | | Normal. |
| 40 | Same | Sterile | Killed 14 days | | Normal. |
| 41 | Same | Sterile | Killed 12 days | Sterile | Normal. |

TABLE VIII.—EFFECT OF INTRAPERITONEAL INJECTION OF DIALYSATES AND CHLOROFORM PRECIPITATES OF AUTOLYZED LIVER

| No. | Material injected | Culture of dialysate | Survival hrs. | Culture of peritoneum at necropsy | Postmortem |
|---|---|---|---|---|---|
| 38 | 100 gm. ground liver incubated 24 hrs. 200 c.cm. water added and dialyzed for 5 days against 16,000 c.cm. water. Dialysate boiled down to 25 c.cm. | Sterile | About 12 | B. welchii | Autolytic peritonitis. |
| 39 | Same but 8,000 c.cm. water used and dialyzed 2 days | Sterile | Survived | | |
| 3 | 42 gm. liver dialyzed 3 days | Sterile | Survived | | |
| 51 | 100 gm. ground autolyzed liver extracted with 500 c.cm. boiling water for 6 hrs. filtered and filtrate treated with $CHCl_3$ in separatory funnel. Precipitates dried and mixed with 25 c.cm. water and injected | Sterile | 18 | B. welchii | Autolytic peritonitis. |

thought that this special strain of bacillus welchii might have a specific virulence, and therefore the following experiment was made. A total of 30 cubic centimeters made up of two mixed litmus milk cultures of bacillus welchii recovered from the peritoneum of a dog were injected intraperitoneally into a normal animal. In spite of the overwhelming nature of this dose in the way of bacteria content, the dog showed absolutely no reaction and was sacrificed 4 days later and the peritoneum found to be sterile.

Group IV. The following attempts were made to determine which factor was in the liver which was capable of bringing about autolytic peritonitis when administered to animals intraperitoneally. Five 100 gram specimens of freshly removed liver were ground, mixed with a small amount of water, and incubated for 24 hours. In each case there was marked gas production and strong putrid odors. The material then was dumped into large flasks and extracted repeatedly with boiling water in amounts up to 5,000 cubic centimeters. This extract was then filtered and the filtrate concentrated by boiling to 25 to 30 cubic centimeters and injected into normal dogs. In each case there was the prompt production of autolytic peritonitis and death.

Group V. An exactly similar set of experiments to Group IV was done, the only difference being that the filtrate instead of being concentrated, was boiled down only to 150 to 250 cubic centimeters. The injection of these filtrates in dilute form into normal animals produced no symptoms whatsoever.

It is clear, therefore, that the toxic factor is a water soluble substance which was thermostable as the material was boiled for a great many hours in the process of concentration as well as the fact that in Groups I and II, material had been autoclaved.

Group VI. Three 100 gram specimens of autoclaved autolyzed livers were extracted for 8 hours in large amounts of boiling water, the water being frequently changed until finally it appeared to contain no more solid material. The left over protein cooked coagulum was then implanted into the abdomens of 3 normal dogs. In each case it produced the typical picture of autolytic peritonitis although one dog lived for 72 hours.

In the next subdivision of this group the same process was followed out except that the

coagulum was further extracted by prolonged boiling with 500 cubic centimeters of alcohol and ether for three changes and then again for three changes of boiling chloroform. This coagulum, after being freed from chloroform by drying, also had the property of producing autolytic peritonitis.

In the latter case it is obvious that the coagulum represents practically pure coagulated protein and that all the lipoid material had been dissolved out by the alcohol and chloroform extractions. Thus the lipoids are removed from consideration as the offending agents. Furthermore it is evident that the practically pure protein left over is able on undergoing autolysis to give rise to toxic products which can in turn produce the autolytic peritonitis. With these points in view it was considered probable that the toxic factor must be a split protein product, probably a proteose or peptone as there is no other substance known to be present and as none of the amino acids would be capable of doing this. This view is further confirmed by experiments in Group VII.

Group VII. Watery extracts of autolyzed livers were made as in Groups IV and V. A study of these extracts showed that they contained large amounts of a nitrogenous material which gave a strong Biuret reaction of the violet type such as is given by substances of the proteose group. There could be no proteins present because the material had been boiled for hours. When boiled with very weak alkali they no longer gave the proteose type of biuret reaction but the bright red color characteristic of peptones. These extracts (see Table VII) in which all the proteose has been autolyzed to peptones or at least lower nitrogeneous substances are no longer toxic.

Group VIII. Watery extracts as prepared above may be freed from their biuret reacting substances by the addition of strong acids or by precipitation with chloroform and partially by precipitation with alcohol, this being a further proof that these substances belong in the peptone proteose group. Material from 100 grams of autolyzed liver was boiled down to a few hundred cubic centimeters and treated with chloroform repeatedly, the precipitate each time being drained out in a separatory funnel. This treatment was continued until no further precipitate occurred on the addition of chloroform. The precipitated material was then freed from chloroform on a water bath and redissolved in a small amount of water. It was shown to be capable of producing autolytic peritonitis.

Other specimens of watery extract were dialyzed against distilled water for varying periods of time and as can be seen (Table VIII) the toxic material is dializable only with great difficulty, as it was fatal in only 1 case.

## CONCLUSIONS

1. In *in vivo* autolysis of the liver, death is due to a condition described as autolytic peritonitis. That is, a toxic reaction characterized by hæmorrhages into the peritoneum with production of much fluid and overwhelming infection with gas bacilli.

2. This reaction can be provoked by the implantation of sterile material.

3. The toxic agent is a water soluble thermostable one which is precipitable by alcohol or chloroform, gives a purple Biuret test, and is with difficulty dializable and therefore probably falls within the albumose group.

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# CLINICAL SURGERY

*FROM THE SURGICAL DEPARTMENT, UNIVERSITY OF PARIS*

## THE JUXTORETROPERONEAL ROUTE IN THE OPERATIVE TREATMENT OF FRACTURE OF THE MALLEOLUS WITH POSTERIOR MARGINAL FRAGMENT

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IN spite of perfection in the technique of reduction in bimalleolar fracture and in spite of the help of roentgen observation in reduction under screen examination, there is a type of malleolar fracture with posterior marginal involvement in which it is impossible to bring about perfect reduction and to maintain reduction once it is accomplished. In these cases operation is necessary and our problem is to determine what is the best incision through which more easily to reach the posterior marginal fragment and fix it.

Dr. Chastang, chief of the surgical service of the Faculty, and I have studied this question in the service of our chief, Professor Pierre Duval.

In France two methods have been proposed: that of Picot[1] who uses the transachillean route after an L-shaped skin flap with the attachment on the inner side is made, and that of Alglave[2] who uses the transcalcanean approach after an L-shaped skin flap attached along the inner border is made. The second method seems to us to be the best, as it gives a better view and makes use of bone section, which is easier to repair than tendon section. Both of these methods have given very excellent results. They have disadvantages, however, in that they necessitate making bone or tendon section and what is even more serious they necessitate cutting a skin flap in a region that is very poorly vascularized, and this procedure may cause gangrene.

Because of these disadvantages we were led to look for some other line of approach that would be less complicated, and we began using the juxtaretroperoneal[3] route which afforded access to the three bones on which it might be necessary to operate: the malleolus lateralis, the posterior marginal fragment, and the malleolus medialis.

[1] Picot. J. de chir., 1923, xxi, No. 5.
[2] Alglave. Bull. et mém. Soc. d. chir., 1923, xlix, No. 35.
[3] Gatellier and Chastang. J. de chir., 1924, xxxiv, 513.

Fig. 1. Position for operation. Note the classical deformity caused by the fracture. Juxtaretroperoneal incision traced.

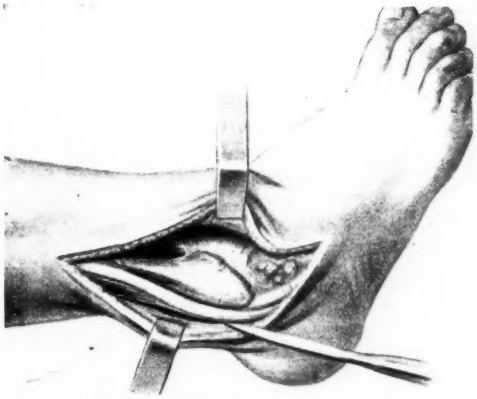


Fig. 2. Separation of the two lips of the incision. Opening of the peroneal tendons.

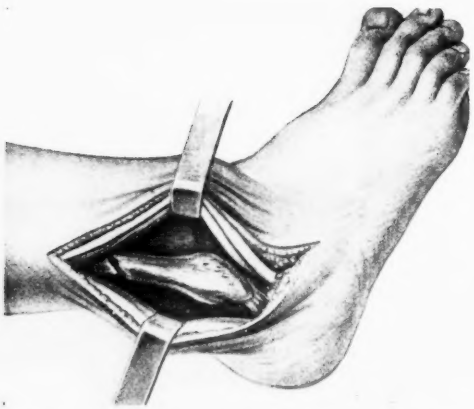


Fig. 3. Pulling the peroneal tendons forward. The fracture of the fibula can be seen.

Fig. 4. The lower fragment of the fibula turned down. The posterior muscles and the tendon of Achilles are held back with a retractor. The posterior marginal fragment is shown. Inspection of the tibiotarsal joint.

TECHNIQUE

The patient is placed in dorsal decubitus with the fractured limb extending some distance beyond the end of the table. Two assistants are necessary: one holds the foot and lower part of the leg and is ready to make any manipulation requested by the operator. We will discuss the treatment of the most complicated type of this fracture—fracture of the fibula between 7 and 12 centimeters from the tip, posterior marginal fracture, fracture of the malleolus of the tibia, separation of the tibia and fibula. The operation is performed through an external incision.

First stage. The skin incision begins 12 centimeters above the tip of the external malleolus, follows the posterior border of the fibula, which is easily found, curves a little forward at the lower end, and runs around the tip of the external malleolus (straight incision curved at the lower end, Fig. 1).

Second stage. The edges of the incision are pulled back, thus exposing the external surface of the fibula and the fractured malleolus, and behind the bone the peroneal tendons in their sheaths can

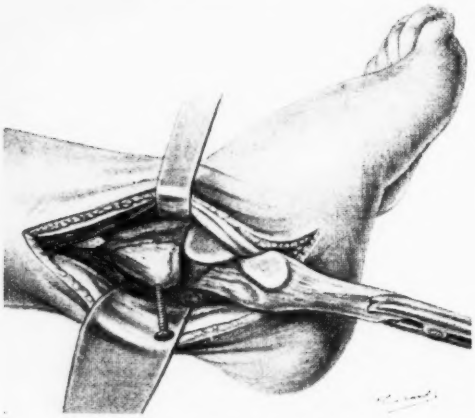


Fig. 5. The foot is put in a varo-equinus position to show the posterior surface of the posterior marginal fragment which is held in place with a screw. Verification of the straight vertical line of the tibiotarsal joint.

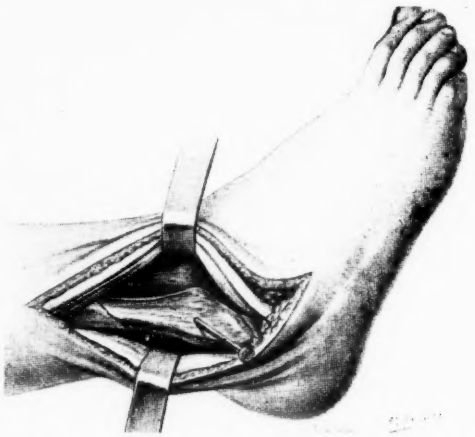
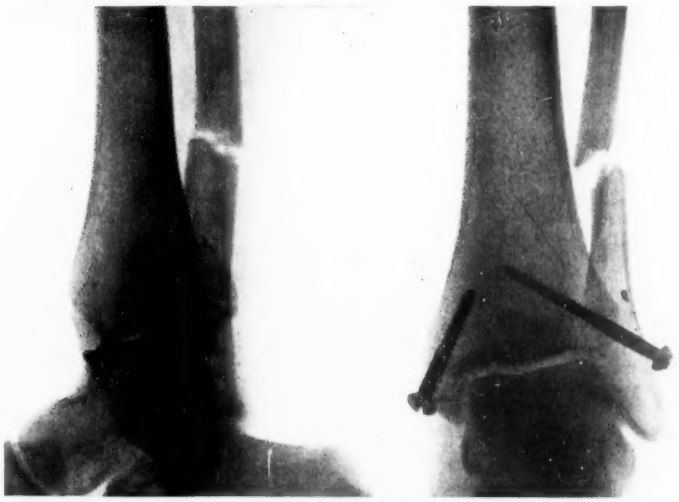
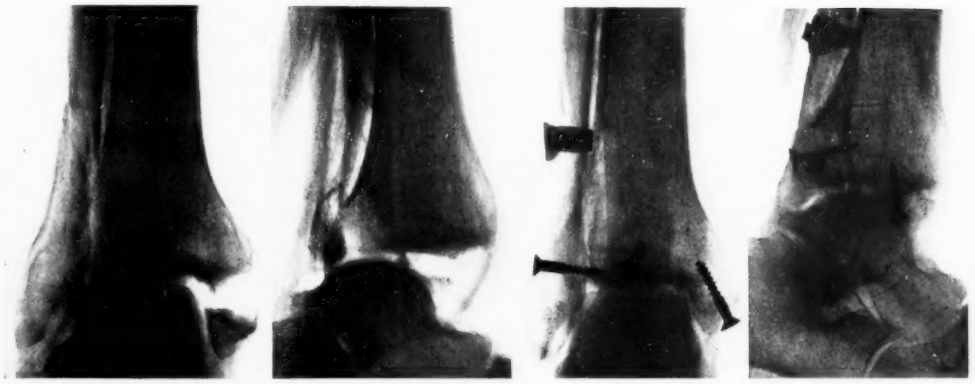


Fig. 6. Restoration to position of the external malleolus which is screwed to the tibia.



Figs. 7 and 8. Bimalleolar fracture with posterior marginal fragment.



Figs. 9 to 12. Results in bimalleolar fracture with free posterior fragment and considerable deformity.

be seen closely applied to the bone. The sheath is sectioned about 2 millimeters from the posterior border of the fibula. This section closely follows the skin incision and runs around the tip of the malleolus. The peroneal tendons are freed from their sheaths (Fig. 2).

Third stage. The peroneal tendons are pulled forward in front of the fibula and are held there with a Farabeuf retractor (Fig. 3). Note that in order to perform this step well it is necessary to detach from the fibula the lowest fibers of the peroneus brevis.

Fourth stage. The lower fibers of the flexor longus hallucis are detached from the posterior surface of the fibula. If the anterior and posterior peroneotibial ligaments are still intact they are sectioned.

Fifth stage. The external malleolus is then turned around its tip from above downward. This manipulation is done without injuring the anterior and posterior peroneo-astragaloid ligaments or the peroneocalcaneal ligament (Fig. 4).

Sixth stage. The assistant holds the foot in forced extension. The tendon of Achilles and the deep posterior muscles of the leg are held downward and backward with a retractor, the peroneal muscles being pulled forward. The field is quite large (Fig. 4) and there can be seen the posterior

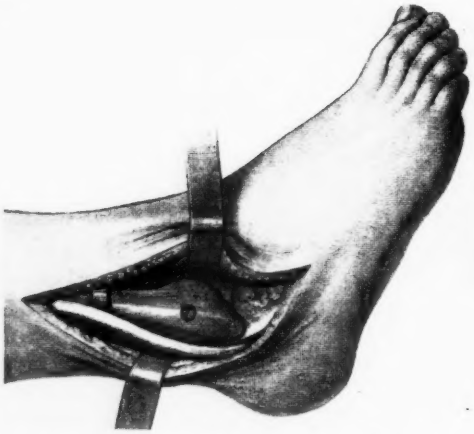


Fig. 13. Osteosynthesis of the fibula with a Parham ring. Restoration to position of the peroneal tendons.

and external surfaces of the lower end of the tibia (lower peroneotibial joint) and the posterior marginal fragment; the peroneal surface of the astragalus; and the joint line, which gapes widely.

Seventh stage. We now clean the joint line, remove the blood clots and small bits of bone, and irrigate with ether.

Eighth stage. We manipulate to reduce the luxation of the astragalus. The internal malleolus may interfere with this reduction. In that case the operator grasps the lower part of the leg with his left hand and the heel and the middle part of the foot with his right (if the fracture is on the right side). Because of the dislocation the repeated friction of the upper surface of the astragalus on the tibia pushes the internal malleolus inward and the reduction is effected. In case of failure a horizontal incision 3 centimeters long can be made below the tip of the internal malleolus; the focus of the fracture is reached and the internal malleolus reduced to the position before we return to the external incision. If the astragalus is properly reduced the fibular surfaces of the tibia and astragalus are plumb. The posterior marginal fragment is now reduced. Evidence of its reduction is furnished by perfect regularity of the joint surface of the tibia, which is well exposed, with the foot in extension and varus.

Ninth stage. The posterior marginal fragment is held in position with a screw. The tendon of Achilles and the tendons of the peroneal muscles must be held well away from the tip. The screw is directed obliquely from behind forward and from below upward (Fig. 5). The external malleolus is next screwed to the tibia, the screw being directed from without inward and from below upward (Fig. 6). Immobilization of the external malleolus is completed by the coaptation of the two fragments (Parham's circle or second tibilfibular screw, depending on whether the fracture is oblique or transverse (Fig. 13).

Figs. 14 and 15. Shows perfect functional result.

Tenth stage. If internal débridement has been necessary the operator returns to the internal wound and sutures the periosteum and the internal malleolus and the skin.

Eleventh stage. He then returns to the external wound, restores the peroneal tendons to their place, sutures the sheath and then the skin.

When the external malleolus and the posterior marginal fragment are in one piece, the external incision is sufficient. In very high fractures of the fibula the operator should not hesitate to section the fibula 7 centimeters above its tip in order to turn it down. In some cases the external malleolus may be attached to the posterior marginal fragment. As reduction of the fibula involves reduction of the marginal fragment a single peroneotibial screw is enough.

## RESULTS

Figures 7 and 8 show a case of bimalleolar fracture with posterior marginal fragment. There was considerable displacement, and non-operative reduction was impossible. The functional result was perfect (Figs. 14 and 15). The movements of the tibiotarsal joint are the same for the two limbs and the imprints of the soles can be superimposed.

The roentgenograms, Figures 9, 10, 11, and 12, show a diagrammatic bimalleolar fracture with a free posterior marginal fragment with considerable deformity, which necessitated both the external retroperoneal and internal tibial incisions. One screw was used for the posterior marginal fragment, one for the external malleolus, and a Parham ring for the fracture of the fibula.

*FROM THE UNIVERSITY OF CALIFORNIA MEDICAL SCHOOL*

# TECHNIQUE OF THE COMPLETE BREAST OPERATION

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THE technical procedure described by Halstead in 1894 marked the earliest efforts to affect a cure of carcinoma of the breast by radical surgery. In the intervening years, various modifications of the Halstead operation have been advocated such as other types of incision of the skin, saving of skin to enable closure without skin grafting, plastic procedures for complete closure, preservation of the muscles, etc., but none of these can be definitely classified as improvements inasmuch as they have lessened rather than enhanced the thoroughness of the procedure. It is the purpose of this article to emphasize the general principles of the original operation and to add a few details which may contribute to a more complete eradication of the disease.

The complete breast operation is indicated in all cases of carcinoma of the breast in which there is any hope of cure by surgical procedure. The earlier the diseased process, the smaller the tumor, and the more hopeful the outlook, the more thorough and painstaking and radical the operation should be. The only hope of cure lies in the complete removal of the growth, that is, the excision of the tumor with a wide margin of healthy tissue and this can be accomplished only before the cancer cells have passed into the inaccessible regions behind the sternum or into more distant regions. Therefore, operations for cancer in its earliest stages must never be limited to partial operations but must represent our best efforts in radical surgery.

There are two objectives in the complete breast operation: first, the complete eradication of the disease, and, second, the restoration of the patient to normal health with normal function of the remaining parts. To accomplish the former there is required a wide excision of skin, an extensive subcutaneous dissection, the removal of the sternal portion of the major pectoral muscle and the complete removal of all the axillary contents except the artery, the vein, and the large nerve trunks (Fig. 1). To attain the latter all axillary dead space must be eliminated and there must be not even the mildest form of infection in skin or subcutaneous tissues after closure of the wound.

## TECHNIQUE OF THE OPERATION

*Step 1. Skin incision and subcutaneous dissection.* A roughly circular incision is usually preferred, depending, of course, somewhat on the location of the tumor in the breast gland. An attempt is always made to give at least 8 to 10 centimeters margin to the tumor, and in all instances all of the skin overlying the breast gland is taken away. This usually means a secondary skin graft or a primary closure by means of a very extensive plastic. The secondary skin graft is undoubtedly the best procedure because it not only insures the widest possible margin to the disease but also gives the best conditions for the proper closure of the axilla.

The incision penetrates the skin and the superficial layers of fat. The skin edges are grasped with Kocher hæmostats, enough of the skin proper being taken in the bite of the clamp to insure the holding. Damage to skin is disregarded because these areas of crushed skin are always cut away at the end of the operation. With these Kocher clamps putting tension on the skin edge, the knife, or preferably the cautery point, is laid against the under surface of the skin and the dissection backward away from the edge is begun (Fig. 2). One always tries to take all the subcutaneous fat off the underside of the skin flaps.

The subcutaneous dissection (Fig. 2) is carried backward until the skin is lifted off the chest wall medialward as far as the opposite border of the sternum, lateralward as far as the lateral border of the scapula, inferiorly to the costal margin, and superiorly to the clavicle. It will be found that this can be accomplished without any splitting of the skin flaps inasmuch as the area of skin removed is quite large and with a little manipulation the far removed recesses of the subcutaneous dissection can be reached.

*Step 2. Chest wall dissection.* Chest wall dissection (Fig. 3) is begun at the superior angle over the clavicular portion of the pectoralis major muscle and carried downward until the dividing line between the clavicular and sternal portion of that muscle is reached. In most instances the line of demarcation is easily seen and in some individuals there are two rather distinct muscles. Occasionally where there seems to be a single muscle the dividing line is located by dissecting downward over the outer surface of the muscle until one strikes some perforating vessels coming through the muscle. These always lie in the plane of

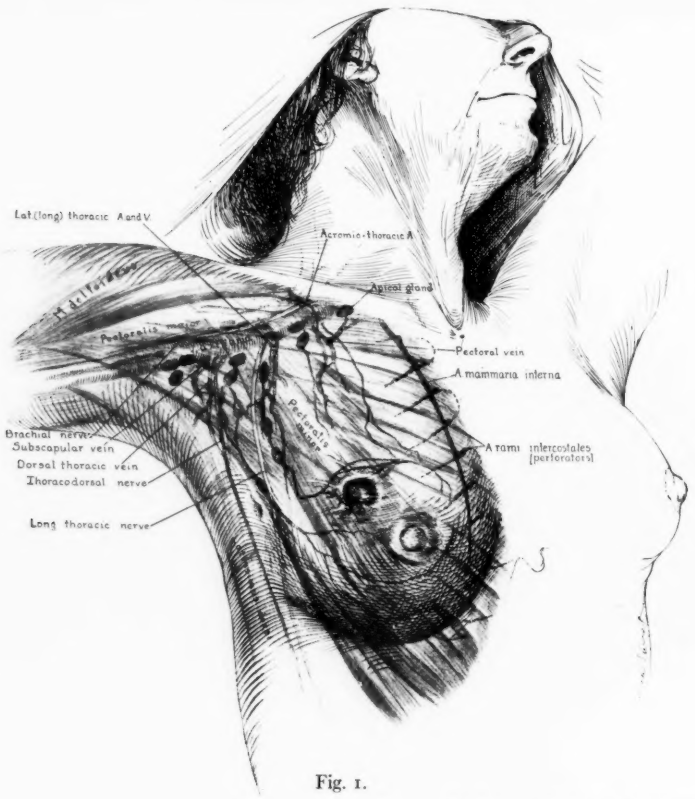


Fig. 1.

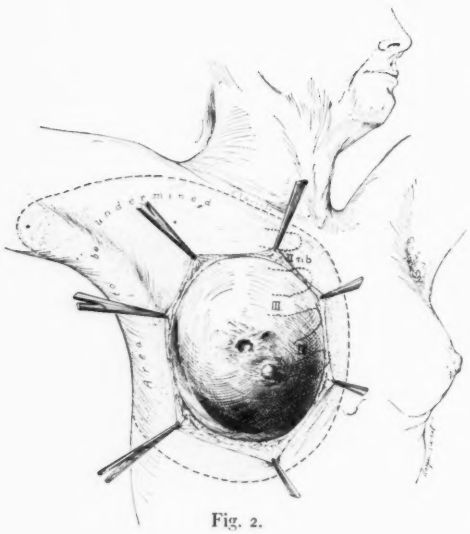


Fig. 2.

Fig. 1. Surface anatomy with transparency showing position of structures to be dealt with in the complete breast operation. The structures to be taken away are the skin overlying the breast gland, the subcutaneous tissues over most of the area shown, the whole major pectoral muscle except the clavicular portion, the lower half of the minor pectoral muscle and the axillary contents. The only axillary structures remaining at the completion of the dissection are the axillary artery, axillary vein, the brachial, the long thoracic and the thoracodorsal nerves. Note the perforating vessels. Lymphatic vessels from the breast penetrate the chest wall along side these vessels to communicate with the retrosternal lymph glands. Note the apical lymph gland at the extreme apex of the axilla (Halstead's gland). Note the glands on the outer surface of the minor above the axillary vessels. These lie along the lymphatic vessels which make a communication between the axillary and cervical glands.

Fig. 2. Amount of skin to be removed in the complete breast operation, the limits of the subcutaneous dissection, and the method of transfixing the skin.

cleavage and the separation of the muscle fibers should be made at this point.

The pectoral muscle attaching to the sternum is then cut away and all of the perforating vessels

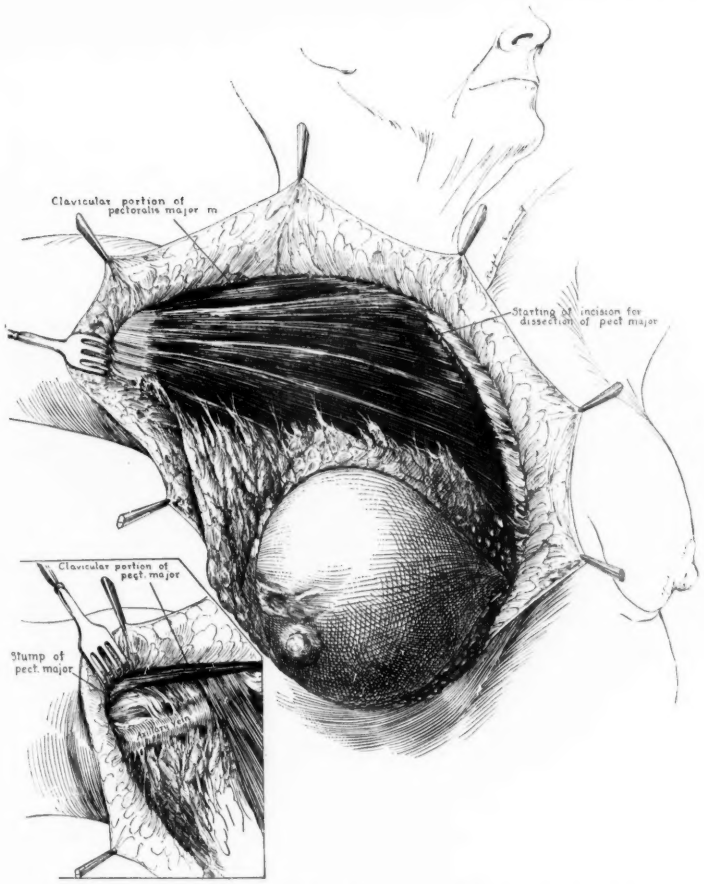
Clavicular portion of pectoralis major m.
Starting of incision for dissection of pect. major
Clavicular portion of pect. major
Stump of pect. major

Fig. 3. Upper and lateral limits of the subcutaneous dissection, the line of demarcation between the clavicular and sternal portions of the major pectoral muscle, the beginning of the division of the major pectoral muscle fibers (vulnerable angle) at the border of the sternum. The whole sternal portion of this muscle is to be taken. The outer end of the muscle is divided 2 centimeters or less from the bone (humerus). Inset shows underlying structures in outer axilla exposed by the removal of the sternal portion of the major pectoral muscle. Relationship of pectoralis minor muscle and clavicular portion of pectoralis major to the axillary contents.

are ligated. This part is done before the axillary dissection because here is the vulnerable angle at which the lymphatics from the breast penetrate through to the mediastinum. It is quite important that these be severed at the very earliest moment so as to prevent the passage, during operation, of the cancer cells by way of these lymphatics into the inaccessible regions.

The dissection is now carried lateralward (Fig. 3) until the insertion of the pectoralis major muscle on the humerus is exposed. When this muscle has been isolated, it is divided as close as possible to the humerus. The leaving of a long stump of this muscle on the humerus always means a visible and a palpable lump which the patient is very likely to suspect is a recurrence of her trouble. The sternal portion of the pectoral major muscle is now freed entirely from the chest wall and laid back to expose the minor pectoral and the axilla (Fig. 4).

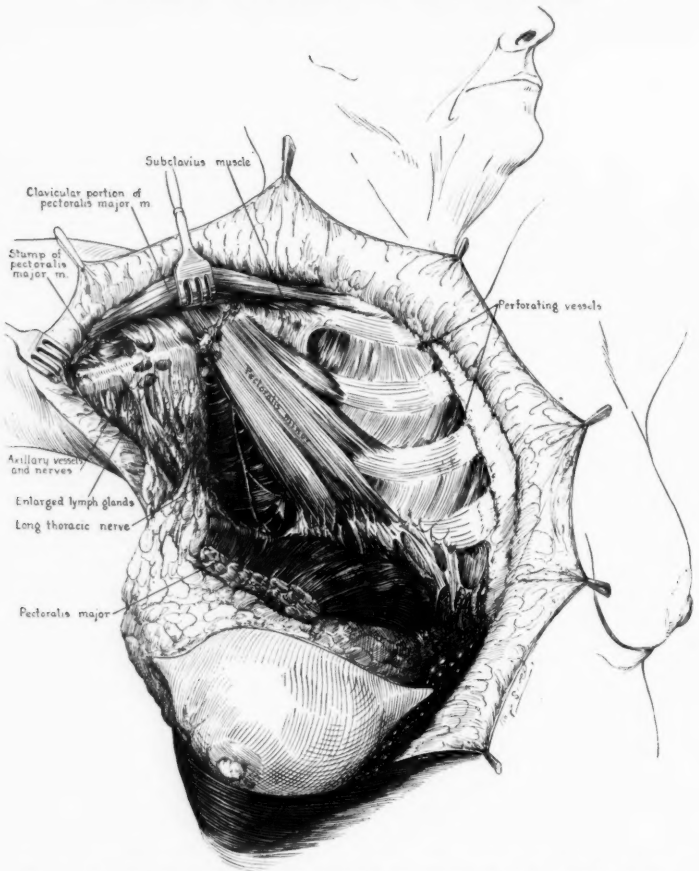


Fig. 4. Immediate and some of the deeper structures to be dealt with after the removal of the sternal portion of the major pectoral muscle. The chest wall dissection up to this point is always done first because the chest wall, especially that portion along the border of the sternum, is the vulnerable area. It is important that the lymphatics paralleling the perforating vessels be divided very early in the operation. This closes the door by which carcinoma cells may pass behind the sternum to inaccessible regions. Note the areolar tissue on the outer surface of the minor pectoral muscle. This contains lymphatic vessels which sometimes form a communication between the axilla and the neck. Also note the subclavius muscle—an important structure in a later stage of the dissection. This muscle arises from the under surface of the middle third of the clavicle and inserts on the anterior surface of the first costal cartilage. It covers the last 2 centimeters of the axillary vein before this vessel disappears behind the clavicle.

The minor is isolated and divided about 5 to 8 centimeters from the coracoid process where it inserts (Fig. 5). The cut ends of the distal portion are grasped with holding forceps, and the muscle is turned back over the clavicle. It serves as a retractor for the skin and for the clavicular portion of the pectoralis major muscle thus exposing the axilla to full view.

*Step 3. Axillary dissection.* First the axillary contents are dissected away from the under surface of the clavicular portion of the pectoralis major at the insertion on the clavicle. As the medial superior border of the clavicle is approached the subclavius muscle is encountered (Fig. 5). It bridges the angle made by the clavicle and first rib and overlies the vein. This muscle is

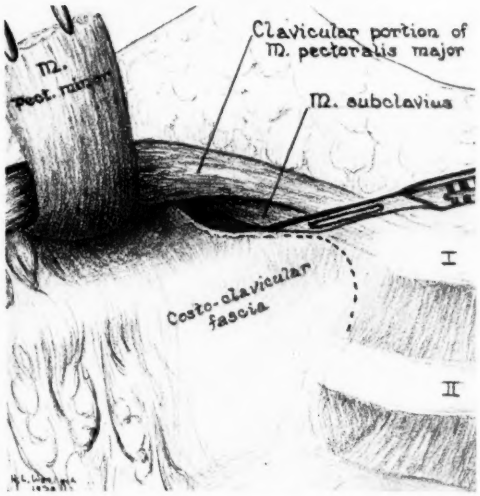


Fig. 5. Showing point of division of pectoralis minor muscle. The muscle acts as a retractor to expose axilla. Showing division of fascia at outer edge of subclavius muscle preliminary to exposure of the axillary vein.

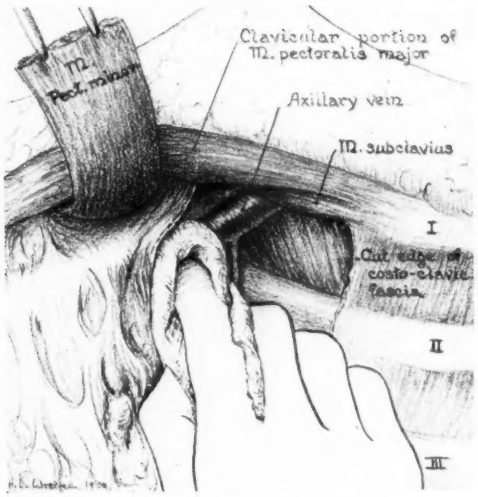


Fig. 6. Illustrating the "wiping down" process after division of fascia with exposure of vein at the clavicle.

cleaned off by dissecting lateralward, or toward the operator, over its outer surface. A tough fascia (Fig. 5) which unites with the outer edge of this muscle flush with its outer surface is nicked with a knife all along the subclavius up to the first rib. This same fascia which spreads out and attaches to the first and second ribs in a plane at right angles to the subclavius is then divided in a horizontal direction thus freeing it from the attachments to the chest wall. This accomplished, a sweeping or wiping outward and downward process quickly exposes (Fig. 6) the vein and the plexus at the superior medial angle of the triangle. This puts the vein at the clavicle in full view and does away with danger of accidental damage to that vessel.

The axilla is now further exposed by a continuation of the wiping down process beginning well up underneath the clavicle cephalad to the vessels and plexus and directed downward at right angles to these structures. Here one is rather early held up by the cephalic vein which empties into the axillary vein superiorly about 2 centimeters from the clavicle. This vessel is usually preserved, simply being cleaned of its loose areolar tissue. Next are encountered some rather sturdy nerve filaments which pass over the vessels. These are divided because they supply the tissue being removed and are of no importance. The wiping down then continues practically without interruptions of any sort until the whole plexus is exposed and until the areolar tissue about the vein is laid bare (Fig. 7).

At this juncture the dissection along the axillary vein is begun. With a rather sharp curved clamp the sheath of the vein is penetrated (Fig. 7) at the point where the vein comes out from under the clavicle. The sheath is then split downward the whole length of the vein over the outer surface. This should accomplish a double purpose. It completely cleans the vein of all lymphatic glands which in some instances lie practically within the sheath of the vein. It also serves to isolate and identify all the branches of the axillary vein at the points of entrance into the vein so that they can be ligated flush against the wall of the axillary vein and before they have been torn (Fig. 7, insert). It is quite important that no stump of these vein branches be left because the clots within these stumps may accidentally, during manipulation of the tissues at operation and during the postoperative movements of the arm, become dislodged and float around in the general circulation. Also such clots might lead to troublesome thromboses of the vein itself.

About 4 centimeters from the clavicle will be encountered an artery crossing over the outer side of the vein. This is the long thoracic artery and should be divided and ligated approximately 1 centimeter from its origin from the axillary artery. The arterial branches are best ligated with a

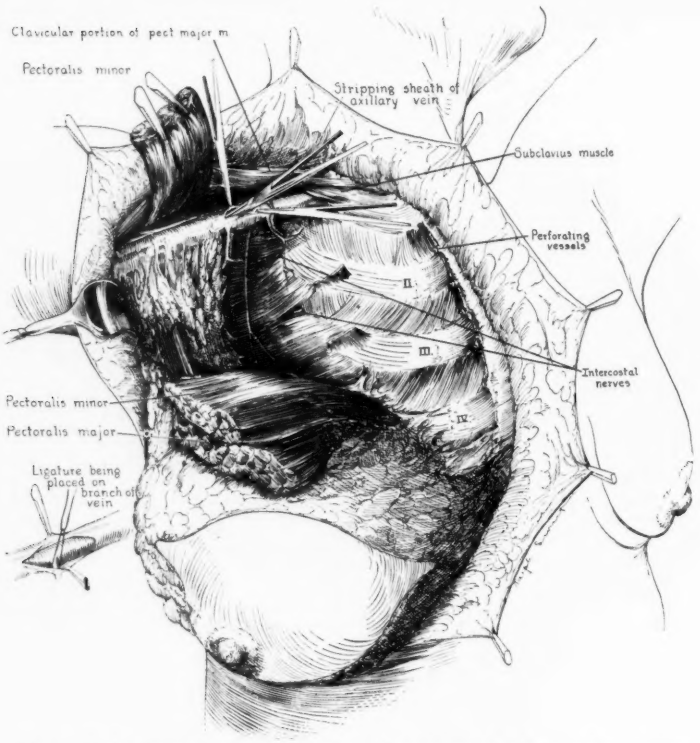


Fig. 7. Early stages of axillary dissection. Note stump of minor used as retractor and the relationship of subclavius muscle to vein. Note the method of stripping the sheath to the axillary vein.

fairly good stump because it is quite important that there be a good thrombus or plug so as to assist in preventing postoperative hæmorrhages. The axillary vein, as a rule, is branched one or more times and all the branches must be carefully followed out until they disappear in the arm. It is well to preserve the axillary vein, but in cases of necessity it may be ligated without fear of ill effects. The largest and most important tributary vessels to be encountered, the thoracodorsal artery and vein, are well out toward the arm. Along with these vessels is a very important nerve, the thoracodorsal nerve, which should be preserved at all costs. Its sure preservation is best accomplished by the isolation and ligation singly of the artery and the vein at the earliest possible moment. Free hæmorrhage from these structures would almost surely result in blind clamping and damage to the nerve.

After the ligation of the branches of the vein and the two arteries named there should be no further hindrance to the rapid clearing out of the remaining, that is, the posterior axillary space. This is accomplished by lifting vein, artery, and plexus on a small retractor and by wiping downward and outward (Fig. 8, insert). Gauze should be used and firm pressure may be applied without fear of damage. Only a few minor veins or arteries will be torn. The ultimate result should be the cleaning off entirely of the subscapularis muscle and the exposure of the long thoracic nerve from end to end.

There remains now the completion of the chest wall dissection. This is somewhat tedious and at times somewhat bloody because the thoracodorsal nerve must be carefully cleaned off. It usually is surrounded by branches of the thoracodorsal artery and vein which may be cut several times before the nerve is entirely freed. The division of either the long thoracic or the thoracodorsal nerve or both causes no permanent disastrous effects but may temporarily cause

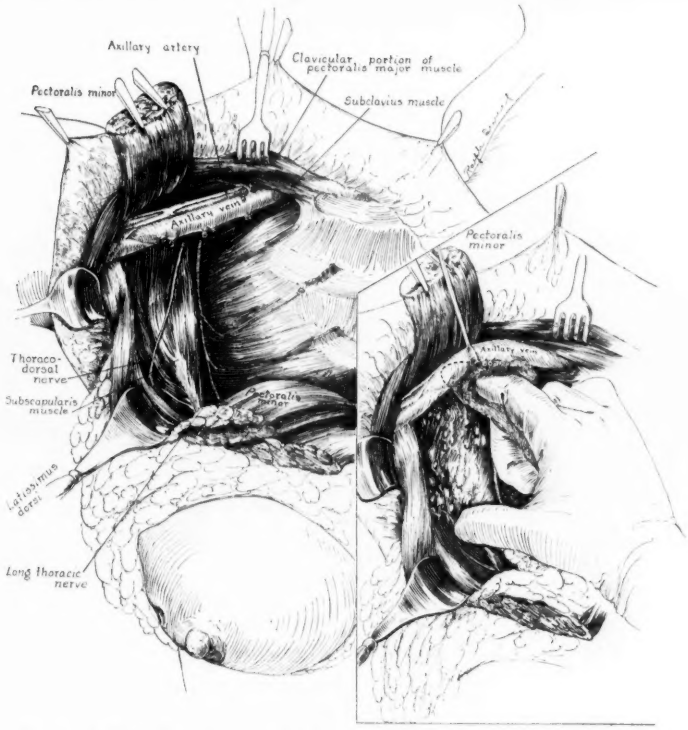


Fig. 8. Axillary dissection completed showing structures remaining. Also showing "wiping down" methods employed for cleaning out the posterior axillary space after the dissection along the vein is completed. This exposes the long thoracic and thoracodorsal nerves, thus avoiding division of these structures in the sharp dissection.

considerable respiratory embarrassment and for some time after, cause the patient to complain of tightness and difficult breathing (Fig. 8).

One or more nerve branches of the intercostals which come out in about the midaxillary line between the upper ribs may cause the operator to hesitate. These must be cut because they cross the axilla or embed themselves in the axillary contents in such a manner that the removal of the axillary contents in one piece cannot otherwise be accomplished. One of these, the intercostohumeral (Fig. 8), sends branches to the arm supplying the integument of the inner surface down as far as the elbow. The division of this nerve gives a very unpleasant hyperæsthesia in its skin distribution which may persist for some time. Also the stump of this nerve may remain very tender causing much distress. On that account the nerve should be cut off very short so that the end retracts between the ribs.

The result should now be as pictured in Figure 9. All the areolar tissue is gone from apex of axilla to costal margin. The walls of the cavity are clean muscle, rib surface and skin flaps. Only the vital nerve and vessel structures remain.

*Closure.* It has often been stated that a surgeon should never close his own wounds, otherwise he may hamper himself by working through too small an incision or may fail to give enough margin to a malignant disease. One must go even further when considering the closure of a complete breast wound. One should never attempt to cover completely over the raw surfaces with skin flaps. Furthermore one should not try to leave as small a grafted area as possible because a large area completely covered with grafts heals as quickly as a smaller area. The only consideration is the complete occlusion of all axillary dead space and the avoidance of sloughing at any point through undue tension. The best results in

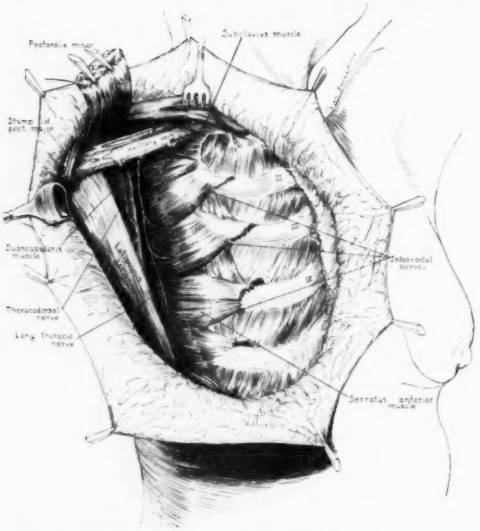


Fig. 9. Radical breast operation completed. All structures shown should be as clearly identified as illustrated and should be as clean of areolar tissue as shown in the sketch. Note especially the relationship of subclavius muscle to the under surface of the clavicular portion of the pectoralis major muscle and to the outer surface of the vein, artery, and nerves. Note the long thoracic and thoracodorsal nerves lying free and undamaged. Note the stump of the pectoralis minor muscle which is now tucked into the dead space above the vessels and nerve plexus.

Fig. 10. Illustrating the arrangement of the skin flaps and the tucking in of the upper flap beneath the vessels and plexus.

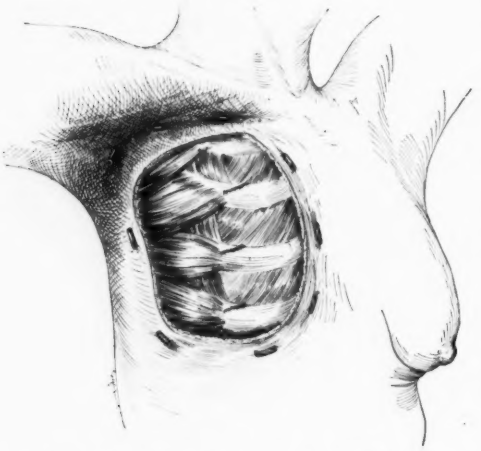

Fig. 11. Closure completed. Note the skin flaps tacked down without tension and the tucked-up superior flap held down by mattress sutures. Note the flat axilla which results. The raw area is to be skin grafted.

closure of the axilla are obtained by Halstead's method described by him in one of his later papers. This consists of the tucking in of the axillary skin flap about the vessels and the maintaining of this position of the axillary flap by means of sutures which tack the skin to the chest wall (Figs. 10 and 11). By this method the minimum of pressure is required and therefore the minimum of bulk of dressings will suffice. In fact the flaps would almost maintain their proper position without dressings at all. A further advantage of this method is the freedom of the arm which is maintained, from the beginning, in full abduction.

The first dressing and skin graft are done on the third or fourth day. With the removal of the dry gauze from the raw area there is a very slight bleeding from the tearing of the fine capillaries which have worked their way into the gauze. This leaves an ideal bed for the grafts. Nitrous oxide is used for a few seconds while the grafts are cut from the thigh. The whole procedure can be done in the patient's room. The upset from the anæsthetic and operation is negligible.

The second dressing is done about 3 or 4 days after the graft. For the remaining 6 or 8 days in the hospital the dressings are changed frequently and usually the wound is healed and without need of further care when the patient goes home on the fourteenth day after the primary operation.

# THE MANAGEMENT OF STONE IN THE SOLITARY KIDNEY AND URETER[1]

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From the Department of Urology, Saint Mary's Hospital

SINCE early times the management of stone in kidney and ureter has been the subject of many articles, discussions, and urological congresses. Although numerous valuable contributions have been made concerning the treatment of stone, relatively few deal with calculus when it occurs in the solitary kidney or ureter due to congenital deformity or disease or surgical removal of its fellow. In operations on the solitary kidney and ureter, drainage of urine from the kidney must be assured at all times and treatment is most exacting. A patient possessing only one kidney is naturally very apprehensive, but he is willing to co-operate with the physician and usually follows any suggestions offered to rid him of stone and prevent recurrence.

In 1916, Beer emphasized that stone in the ureter of a solitary kidney should be removed by ureterolithotomy, rather than by attempts to remove it or cause it to pass by cystoscopic manipulation. In 1930, Keyes reported 5 cases on whom he had successfully removed calculi from the remaining kidney. Walters stated that in the 43 patients on whom an operation was performed on the solitary kidney and ureter at the Mayo Clinic, there was a mortality of 14 per cent and he stressed early intervention before renal insufficiency had set in making the patient a poor surgical risk. The management of stone-producing patients presenting a solitary kidney calls for intelligent employment of several prophylactic measures, earlier surgical intervention, the most exacting operative technique, and keen surgical judgment. In performing 13 operations for various pathological lesions in the solitary kidney and ureter, I was impressed by the lack of shock attending or following the surgical intervention. These consisted of one nephrolithotomy, one pyelonephrotomy, two ureterolithotomies, two nephropexies, two renal abscesses in which drainage was made, one decapsulation, and four ureterostomies into the skin of the lower abdomen one of which consisted of the implantation of a double ureter.

Having treated four patients in whom stones were found in a solitary kidney and ureter, I herewith present my cases:

Case 1. E. S., a man, aged 58 years, a cobbler, referred by Dr. Donald MacGedge, entered the hospital December 8, 1928, with complete urinary retention accompanied by fever, pain, and swelling in the region of the right kidney. At the age of 37 years he had had a nephrolithotomy for calculi in the left kidney; at 53 years a lithotripsy for bladder stone was done; at 54 years removal of a hypertrophied prostate and 6 months later left-sided nephrectomy were done for pyonephrosis with recurrent stone formation in the kidney; and at 55 years I removed a calculus from the upper calyx of the remaining kidney by a nephrolithotomy incision. In order not to disturb the kidney the left rib was resected. Subsequent X-rays revealed the absence of stone. Later, however, he passed several small stones and, for the reason that it was thought that the chronic pyelonephritis present in the right kidney was a great factor in stone formation in his case, renal lavage and dilatation of the ureter were done at intervals for the purpose of reducing this infection and maintaining a wide passage in the right ureter. On December 7 he was suddenly taken with complete urinary retention, pain in the right lumbar region, chill followed by fever, and the appearance of a large mass in the right upper abdominal quadrant. A roentgenogram was made; on account of gas in the intestines no shadows suggestive of calculi were seen. The right ureter was catheterized and an obstruction was encountered 7 centimeters from the orifice, which was finally passed, liberating approximately 18 cubic centimeters of purulent urine under pressure. Following this ureteral manipulation a stone measuring 6 millimeters in diameter passed into the bladder and was removed by cystoscopic rongeur forceps. Although good drainage had been established, the enlarged right kidney did not recede in size and for this reason surgical intervention was made. The kidney on being exposed was found to contain numerous miliary cortical abscesses on its convex surface. These varied from 2 to 5 millimeters in diameter and seemed to involve the entire kidney. We realized that we were dealing with sudden invasion of the cortex by an infection that had been present in the pelvis of the kidney over a period of years. The superficial abscesses were drained with little hope for improvement. A number of transfusions were given; however, the creatinine of the blood gradually climbed from 2.6 millimeters to 6 millimeters per hundred cubic centimeters and in 2 weeks' time the patient succumbed.

This case exemplifies the importance of early surgical removal of a stone blocking the ureter of a remaining kidney, particularly when the latter is infected. Had we seen this patient 36 hours sooner, before complete obstruction of the ureter had taken place, the removal of the stone would have prevented the invasion of the cortex of the kidney by infecting organisms that had been present in the pelvis over a period of years, and saved the patient's life.

Case 2. W. I., hospital No. 51539, a man, aged 26 years, cheese salesman, referred by Dr. W. Lynch, entered St. Mary's Hospital, April 27, 1928, with repeated attacks of dull pain in the region of the left kidney, loss of weight, and

[1]Read before the General Meeting of the San Francisco Medical Society, May 13, 1930

marked weakness. His symptoms began at the age of 21 years, ureteral calculi were diagnosed in the lower left ureter at the age of 23 years and seven calculi were removed from the left ureter by ureterolithotomy at the age of 25 years. At the same time bilateral meatotomy of the ureteral orifices was also performed through the open bladder. Examination revealed a left pyonephrotic kidney containing a large coral-type calculus in its upper pole and a smaller calculus in the lower pole, a large calculus in the lower portion of the left ureter, and a huge right-sided hydronephrosis. In performing the phenolsulphonephthalein test (intramuscular) 50 per cent was recovered in 2 hours. After being injected intravenously indigocarmine appeared of a dark blue color in 5 minutes on the right side and faintly in 7 minutes on the left side and remained very pale for 30 minutes. On May 10, 1928, a complete left ureteronephrectomy was made and a pyonephrotic kidney containing large stones and a ureter containing two stones measuring 3 centimeters by 1.5 centimeters were removed. The patient made an uneventful recovery but the pyelonephritis which had always been present in the opposite kidney persisted. As it was thought to be a factor in stone formation in his case, renal lavage with 1 per cent mercurochrome and dilatation of the ureter were done at intervals for the purpose of reducing this infection and maintaining a wide passage in the ureter. A roentgenogram made on October 15, 1928, revealed a calculus about 1 centimeter in diameter in the lower pole of the right kidney and a larger stone in the right ureter. Succussion was applied after the manner described by Bransford Lewis and a radiogram made 3 days later demonstrated that the renal calculus had passed out of the kidney pelvis into the ureter lodging just above the intramural portion of the ureter below the larger stone. The ureteral orifice was widened by further slitting with a scissors and the ureters dilated with bougies, but it was soon seen that the calculi were too large to pass by the lower portion of the ureter. On January 7, 1929, a ureterolithotomy was performed and two calculi 1.5 centimeters in diameter were removed from the pelvic portion of the ureter. The wound healed in 11 days and convalescence was uneventful. A roentgenogram made on April 15, 1930, was negative for stone and the urine analyzed on that date was negative.

This case exemplifies the tendency of certain patients to form calculi even in spite of all measures taken to eliminate stasis and to eradicate infection. This also demonstrates the lack of shock attending operation for stone on the remaining ureter, provided the patient has been properly prepared.

CASE 3. L. H., hospital No. 61449, a man, aged 32 years, a plumber, entered St. Mary's Hospital April 20, 1930, with complete urinary retention associated with vomiting, hiccough, pain, and swelling in the region of the right kidney. At the age of 29 years he was treated for ureteral stones of the left ureter. Following cystoscopic manipulations consisting of meatotomy of the orifice and dilatation of the left ureter a number of stones were passed. These procedures gave temporary relief and on December 20, 1929, I removed the left kidney and ureter because of tuberculous pyonephrosis with stone formation, ureteritis, advanced stricture formation, and impacted stones in the left ureter. The lumbar incision was slow in healing, developed a lumbar sinus which was later resected and allowed to heal by secondary intention. On April 12, 1930, he developed an attack of severe renal crisis in the solitary kidney followed by the passage of two small stones. On April 20, he developed a similar attack accompanied by complete urinary retention. A radiograph revealed a calculus in the region of the lower portion of the right ureter. Early the following day cystoscopy was performed for the purpose of passing a catheter by the obstructing calculus in order to establish drainage of urine. A stone 4 millimeters in diameter was seen to impact and completely obstruct the intramural portion of the ureter. By this time the right kidney had increased in size and palpation revealed that it had become considerably enlarged, apparently from an accumulation of urine in the pelvis. The stone was dislodged by the aid of a bougie. In changing its axis a gush of urine was seen to flow from the occluded orifice after which the patient experienced immediate relief from the sense of fullness and pain in the kidney above. As the patient had been dehydrated from constant vomiting, it was deemed best to give him fluids by means of hyperdermoclysis under the pectoral muscles. Three or 4 hours were allowed for absorption of water after which I contemplated removal of the calculus in the lower ureter by ureterolithotomy. Ten minutes before the patient was to have been brought to the operating table the stone passed from the lower ureter into the bladder and was voided spontaneously. A roentgenogram was taken and revealed that the stone had passed.

This case exemplifies the predisposition of certain patients to form stones even after a pyonephrotic kidney and ureter had been removed on the opposite side. It also emphasizes the importance of early surgical intervention in cases presenting complete obstruction due to stone in the remaining ureter. Although it was impossible to pass by the stone by introducing bougies, these manipulations changed the axis of the stone, allowing urine to pass and relieve the back-pressure present in the kidney, culminating in actual passage of the stone.

CASE 4. Mrs. M. H., hospital No. 40429, housewife, aged 60 years, entered St. Mary's Hospital June 20, 1926, complaining of pain in both kidney regions, increased frequency, dysuria, loss of weight, and weakness. Urological examination revealed two calculi in the lower portion of the right ureter and an impacted calculus in the lower portion of the left ureter, completely obstructing the outflow of urine. No function was found to be present in the left kidney and it was concluded that it was entirely destroyed by a pyonephrotic process. On May 21, 1926, a right-sided ureterolithotomy was performed. On September 15, 1926, a left-sided ureteronephrectomy was made for pyonephrosis, ureteral stone, and ureteritis with complete closure of the ureter. Three years later she developed characteristic symptoms of advanced rebellious cystitis and hydronephrosis of the remaining kidney and in spite of repeated dilatations of the bladder and ureter under anæsthesia, the bladder contracted to 30 cubic centimeters, and the lower portion of the right ureter became greatly constricted. On June 3, 1929, a right-sided temporary nephrostomy was performed as a preliminary step to ureterostomy into the skin of the lower abdomen. The patient received such benefit from nephrostomy that ureteral transplantation has been postponed to a later date.

Because of dense peri-ureteral adhesions and marked tortuosity of the ureter it was necessary to make the incision into the ureter directly over the stone in order to

locate it for removal. Undoubtedly this incision into the portion of the ureter that had undergone cicatricial changes aided in subsequent stricture formation resulting in almost complete closure.

CASE 5. H. T., hospital No. 28428, a man, aged 45 years, former middle weight prize fighter, entered St. Mary's Hospital February 11, 1924, complaining of pain and swelling in the region of the right kidney, the passage of gravel, hæmaturia, dysuria, œdema of eyelids, loss of weight, and weakness. At the age of 43 years a number of calculi passed from the right ureter following cystoscopic maneuvers consisting of meatotomy of the ureteral orifice and progressive dilatation of the ureter with bougies. In performing the phenolsulphonephthalein test 50 per cent was recovered in 2 hours after intramuscular injection. A roentgenogram revealed a calculus in the left kidney pelvis, an impacted stone in the right lower ureter, bilateral pyelonephritis and hydro-ureter, and hydronephrosis on the right side. Twelve and one-half per cent phenolsulphonephthalein was recovered from the right ureter and 5 per cent from the left ureter in one-half hour after intravenous injection. Operation was advised, it being my purpose to remove the calculus from the left kidney in which the infection was less than in its fellow. Operation was refused and subsequent examination on October 6, 1924, revealed a calculus forming in the right kidney pelvis. Bilateral meatotomy and renal lavages were performed and progressive dilatations of the ureters were made following which the patient passed dozens of stones from the right kidney, the largest of which measured 1 centimeter in diameter. On October 21, 1924, a piece of one of the stones (which had rapidly increased in size and number in the right kidney) passed down the ureter and completely obstructed it. The patient presented huge swelling in the kidney region, ran a high fever, and was toxic. In spite of drainage of pure pus obtained by passing two No. 6 Charrière ureteral catheters beyond the obstructing stone, the patient became more toxic and progressively weaker. On September 26, 1924, a nephrectomy was performed and a large pyonephrotic kidney containing numerous calculi, the largest 5 centimeters in diameter, was removed. The ureteral calculus was grasped by a long forceps and removed through an opening in the ureter. The convalescence was somewhat stormy and the patient left the hospital 3 weeks later. Since that time repeated roentgenograms have been taken of the remaining left kidney. It has greatly hypertrophied and the calculus contained therein has taken on a coral shape and has almost entirely filled the pelvis and calyces and on February 6, 1930, measured approximately 8 by 3 centimeters. This calculus is apparently of a harder nature than those that had been present in the right kidney as no pieces have broken off. There has been no obstruction of the left ureter nor passage of small calculi. The patient has refused operation on the remaining kidney and in spite of the huge stone in his solitary kidney enjoys fair health some 6 years after nephrectomy for right-sided calculus pyonephrosis.

This case exemplifies the importance of early surgical intervention for stone before renal insufficiency and advanced infection has set in, thus making the patient a poor surgical risk. It also demonstrates that stones, coral-form or otherwise, in which fragments separate and pass down the ureter should be removed at once. They might completely obstruct the ureter and in kidneys presenting chronic pyelonephritis cause invasion of the cortex by the infecting organisms present, resulting in complete destruction of this organ.

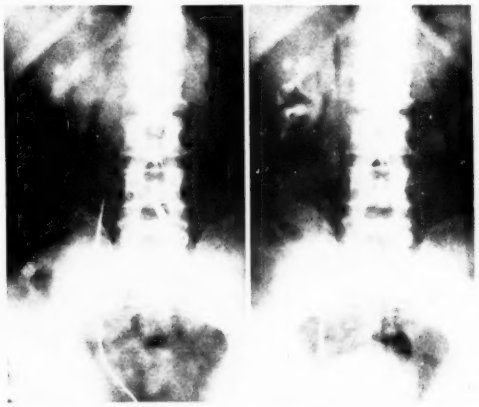
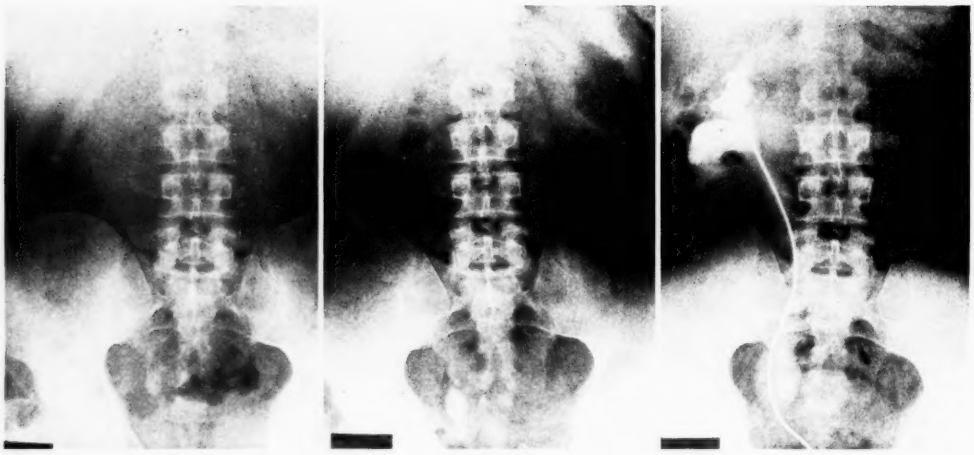


Fig. 1. A, left. Male, aged 53 years. Roentgenogram showing round shadow in region of upper pole of solitary right kidney. Opposite kidney previously removed for recurrent calculi and pyonephrosis. B, Pyelogram localizing calculus in upper major calyx. Successfully removed by nephrotomy. Case 1.

CASE 6. M. O'B., hospital No. 29376, a man, aged 29 years, laborer, entered St. Mary's Hospital January 10, 1929, complaining of frequency, persistent pyuria, dizziness, and palpation of the heart of 5 years' duration. Seventy per cent phenolsulphonephthalein was recovered in 2 hours after intramuscular injection. Roentgenographic examination revealed two irregular calculi in the upper and middle calyces of the right kidney and absence of the left kidney. The ureter above the left orifice in the bladder was completely closed. Urines collected from the right kidney and bladder showed numerous leucocytes, erythrocytes, colon bacilli and staphylococci, and were negative for tuberculosis. On January 28, 1929, both calculi were removed from the upper and middle calyces of an enlarged kidney apparently due to compensatory hypertrophy by a pyelonephrotomy incision. An abscess was found in the lower pole which was also opened and drained. No hæmorrhage followed, and although the incision did not heal for 8 weeks, it was finally closed by the employment of indwelling catheters. Subsequently the pelvis was treated by renal lavage. The urine has greatly improved and a radiograph taken in February, 1930, was negative for stone.

## TREATMENT

The treatment of stones in the solitary kidney and ureter can be divided into prophylactic and surgical. When it has been necessary to remove a kidney because of calculus pyonephrosis, be it due to advanced infection or the formation of abscesses resulting in more or less complete destruction of the parenchyma, one should divert his attention to certain prophylactic measures preventing the formation of stone in the healthy fellow. In a given case of bilateral renal calculi in which one kidney is destroyed by advanced infection or hydronephrotic atrophy, surgical attack should first be directed to the removal of the



A. B. C.

Fig. 2. A, Male, aged 26 years. Roentgenogram showing recurrent calculus in lower ureter and formation of a new calculus in solitary kidney. Opposite kidney and ureter removed because of recurrent calculi formation and pyonephrosis. B, Roentgenogram taken 3 months later showing passage of kidney stone following succussion. One can observe the new position taken by this calculus which is below the larger ureteral stone. C, Ureteropyelogram showing position of the stones in the ureter. Calculi removed by ureterolithotomy. On April 15, 1930, the urine was negative and a roentgenogram taken at that time showed no calculi. There is a clinical relief of symptoms. All possible foci of infection have been removed. Case 2.

calculus from the functioning kidney, and at a later date the other useless kidney should be removed.

*Prophylactic.* In certain cases of nephrolithiases early nephrectomy for calculus pyonephrosis removes the focus of infection which is often the cause of infection and stone formation in the opposite kidney (Nicolich, Rovsing, and Rafin). Roentgenograms should be repeatedly taken at intervals in order immediately to detect recurrence or the formation of a new stone. The urine should likewise be examined monthly for pus and blood, the presence of which points to infection with or without stone. The finding of macroscopic or microscopic blood without pus usually indicates the recurrence of calculi. All foci of infection should be eliminated; diseased tonsils should be removed, abscessed teeth extracted, infected sinuses drained, and infections in the prostate, seminal vesicles, uterus, tubes, and ovaries eradicated. Likewise, infections in the bladder should be cleared up. Because of the great rôle of stasis in the formation of stone one should make sure that the drainage of urine is unimpeded. Obstructions in the lower tract should be relieved, urethral strictures should be dilated, an obstructing prostate should be removed, and median bars should be tunneled by the electrocautery or punch operation. Congenital stricture of the ureteral meatus should be divided by the cystoscopic scissors or fulguration. Hunner has called attention to the rôle of ureteral stricture in the formation of kidney stone. Progressive dilatation of the ureters should be made in all cases of congenital and acquired stricture. Stasis of the kidney due to ptosis should be relieved by nephropexy and congenital constrictions of the ureteropelvic junction should be corrected by the proper plastic operation. Extra-ureteral pressure caused by anomalous vessels should be relieved by resection of the obstructing vessel. Lesions of the pelvic organs which encroach upon and obstruct the ureter should be surgically removed. Infection of the remaining kidney should be systematically and energetically eradicated. Pelvic lavage should be employed until the kidney is freed from infection. In performing kidney lavage in patients prone to stone formation, one may not employ silver nitrate as it tends to aid the formation of stone by depositing silver chloride on any nucleus that might be present, be it bacteria, mucus, etc. It is better to employ rivanol, 1:4000, the albuminoid silver salts, mercurochrome 220 (½ to 1 per cent) etc. Obstinate cases can be greatly benefited by the local injection of the bouillon filtrate of an autogenous vaccine prepared from the patient. It contains an antivirus, is injected directly into the pelvis, and acts by virtue of its local immunizing

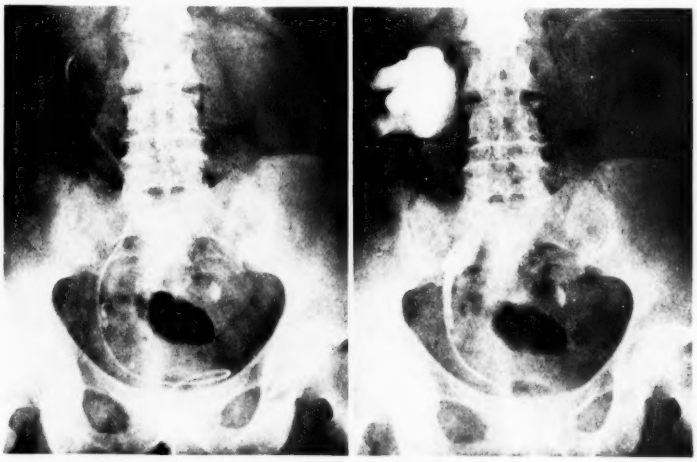


Fig. 3. A, left. Female, aged 60 years. Roentgenogram showing calculi in the right lower ureter in apposition with the opaque catheter. Opposite kidney destroyed by complete obstruction due to calculus in lower ureter which is seen in left side of bony pelvis. B, Ureteropyelogram localizing calculi in ureter and demonstrating hydro-ureter and hydronephrosis. Calculi of right ureter removed by ureterolithotomy. Left pyonephrotic kidney and ureter removed at later date. Case 4.

power. The patient should be placed on a low protein diet, advised to abstain from irritating rich foods, and to drink distilled water. In their zeal to combat acidity and to prevent stone formation some patients take in alkaline producing vegetables, citrous fruits and alkaline waters, etc., in excess overloading the urine with crystaloids favoring the formation of stone.

### TREATMENT OF STONE IN THE SOLITARY KIDNEY

When one is called to deal with stone in the solitary kidney all efforts possible should be directed toward conservation of renal tissue. Drainage of urine from the kidney must be assured at all times as there is no opposite kidney to fall back upon for elimination of waste products. Surgical procedures must be of a nature to assure the integrity and unimpairment of as much renal tissue as possible. In attacking the kidney surgically, great care and gentleness should be exercised in exposing the kidney as the least accident might prove fatal. In attacking the kidney one should avoid sacrificing blood vessels which would interfere with the nutrition of the kidney. If the stone is located in the upper pole one should not hesitate to resect the last rib facilitating the approach and removal of the stone. In such cases the calculus can often be removed without delivering the kidney into the incision. One must be certain not to leave any fragments which might act as a nucleus for future stone formation. If the stone is located in the pelvis, is smooth, and easily accessible it can be removed by a simple pyelotomy incision. If it is located in one of the calyces its removal through a pyelotomy incision might cause one to leave a fragment which will act as a nucleus and aid in

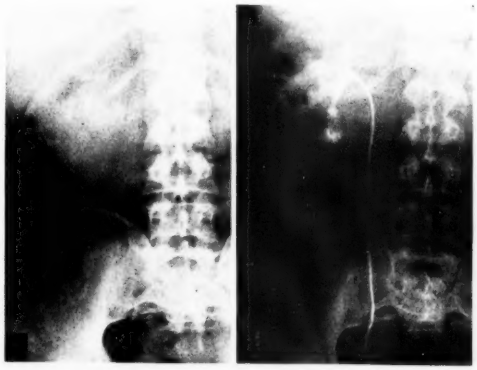


Fig. 4. A, left. Man, aged 29 years, presenting irregular shadows in region of middle portion and upper pole of congenital solitary right kidney. B, Ureteropyelogram localizing these calculi and demonstrating an abscess of the lower pole. Stones removed by pyelonephrotomy and abscess of lower portion drained at time of operation. Clinical relief of symptoms and no recurrence of stone to date. Case 6.

Fig. 5. Ureterolithotomy for calculus situated low down in the pelvic portion of the ureter. When possible the stone is milked up into the incision or grasped by a long forceps which facilitates the operation. Incision in the healthy portion of the ureter assures better healing and less subsequent stricture formation.

future stone formation. I have noted the reformation of stone in 3 patients in whom the stone was removed by the aid of a forceps from a calyx through the pyelotomy incision. Unquestionably, a small fragment was left behind. The employment of fluoroscopy as suggested by Braasch and Carman and the taking of films at the time of operation (Quinby) is a great aid in localizing and assuring the removal of all stones and fragments. A stone in a major or minor calyx is best removed by making a combination pyelotomy and nephrotomy incision. The pelvis is opened sufficiently to allow one to insert the index or little finger. The stone is palpated and kept in place by firm gentle pressure. At the same time it is located from without by the aid of a small groove director or blunt needle which acts as a guide for opening the parenchyma with a silver wire. The stone is then extracted with forceps or pushed out from its bed by the finger below. In this manner there is less likelihood of breaking off or leaving fragments. If the stone is of soft consistency and there is a likelihood of its being broken a thorough lavage is made of the pelvis in order to wash away small particles. The pyelotomy incision should not be closed by suture thereby assuring good drainage. After the operation partial decapsulation is performed in advanced cases in order to minimize postoperative renal congestion. Partial decapsulation is performed by incising the capsule and separating it from the kidney with the finger for a slight distance only. This assures the minimum amount of kidney surface adhering to the surrounding structures and facilitates surgical approach should it become necessary to operate on the kidney at a future date. One is impressed by the lack of shock and the absence of any alarming diminution of renal function after this operation.

TABLE I.—PROPHYLACTIC MEASURES IN THE TREATMENT OF CALCULUS IN SOLITARY KIDNEY AND URETER

1. Early removal of unilateral calculi and calculus pyonephrosis.
2. Clearing up of foci of infection:
   - A. Furuncles, boils, and carbuncles—open drainage.
   - B. Infected tonsils—tonsillectomy.
   - C. Infection of sinuses and ear—open drainage.
   - D. Abscessed and pulpless teeth—extraction.
   - E. Infected prostate and seminal vesicles—routine massage, surgical drainage.
   - F. Infected genital organs in women—removal of infected tubes, cauterization of cervical glands, etc.
3. Clearing up of stasis:
   - A. Upper urinary tract.
     1. Meatotomy of ureteral orifice.
     2. Progressive dilatation of ureter.
     3. Removal of extra-ureteral pressure: anomalous vessels and lesions of genital organs in the female.
     4. Increased mobility with kinking of ureter—support with belt, nephropexy.
     5. Surgical correction of obstructions at ureteropelvic junction.
   - B. Lower urinary tract.
     1. Urethral stricture—dilatation, urethrotomy.
     2. Median bar vesicai neck—electrocautery, punch operation, open operation.
     3. Hypertrophied prostate—prostatectomy.
     4. Bladder stone—lithotripsy—cystolithotomy.
4. Clearing up of chronic pyelonephritis:
   - A. Renal drainage and lavage at intervals.
   - B. Lavage of bladder to minimize reinfection of kidneys.
   - C. Internal and intravenous administration of urinary antiseptics.
   - D. Vaccinotherapy—local immunization by injection of filtrate directly into renal pelvis.
5. Regimen:
   - A. Bland, low protein diet.
   - B. Intake of distilled water only.
   - C. Prohibition of excesses in drinking and eating.
6. Prophylactic examination of patient:
   - A. Roentgenograms of entire urinary tract every 3 to 6 months.
   - B. Monthly complete urine analysis.

Unfortunately, operation for stone in the solitary kidney is often delayed because of ignorance on the part of the profession as to its relative safety. Patients are allowed to go on until irreparable damage has taken place, transforming a good subject for surgical relief into a hazardous risk.

### TREATMENT OF URETERAL STONE

It is a well proved fact that about 90 per cent of ureteral stones can be caused to pass by cystoscopic maneuvers such as meatotomy of the ureteral orifice, dilatation of the ureter by means of catheters and bougies, rubber bags, mechanical dilators, etc. Excepting in the patient presenting impacted and unduly large stones and in cases of

TABLE II.—OPERATIONS ON SOLITARY KIDNEY AND URETER

| | Cases |
|---|---|
| Nephrolithotomy for stone | 1 |
| Pyelonephrotomy for stone | 1 |
| Ureterolithotomy for stone | 2 |
| Nephropexy | 2 |
| Renal abscess | 2 |
| Decapsulation of kidney | 1 |
| Ureterostomy into skin lower abdomen | 3 |
| Ureterostomy of double ureter into skin | 1 |
| Total | 13 |

TABLE III.—TREATMENT OF STONE IN SOLITARY KIDNEY

1. Cystoscopic maneuvers to cause passage of stone—dangerous. Rarely employed.
2. Surgical points in technique:
   - A. Wide incision, resection of last rib for larger exposure.
   - B. Extreme gentleness.
   - C. Avoid sacrificing blood vessels.
   - D. Pyelotomy for smooth stones in pelvis.
   - E. Pyelonephrotomy for large irregular stones and those in calyces.
   - F. Pyelotomy incision not sutured.
   - G. Decapsulation.

TABLE IV.—TREATMENT OF STONE IN SOLITARY URETER

1. Cases very limited in which cystoscopic maneuvers can be safely utilized. Danger of obstruction and anuria.
2. Surgical points in technique:
   - A. Preliminary drainage and lavage of pelvis through ureteral catheter.
   - B. Retention catheter at time of operation.
   - C. Incision in ureter above side of stone and stone removed by forceps or milking.
   - D. Ureterotomy incision not sutured.
   - E. Careful replacement of ureter to prevent undue angulation.

advanced infection the efficacy of this procedure is without question. Following dilatation of the ureter by bougies, the actual descent of the stone is brought about by changing the axis of the stone or by the propulsive force of the urine. This is in a measure due to œdema caused by instrumentation at the site of the obstructing stone (Beer). The resulting increased pressure behind the stone acts as a driving force. When stone occurs in the solitary ureter such blockage of the passage over an appreciable length of time causes anuria and results in rapidly forming uræmia and death. If there has been pre-existing infection in the kidney in the form of pyelonephritis, this back pressure will often cause involvement of the parenchyma by the infecting organisms present resulting in acute suppurative nephritis with the formation of multiple cortical abscesses. This pathological process is well exemplified in Cases 1 and 4 in

which a calculus completely blocked the ureter resulting in invasion of the cortex by an infection that had been present in the pelvis for years forming multiple miliary abscesses entirely destroying the parenchyma resulting in destruction of the kidney in one and in uræmia and death in the other.

One should attempt to establish preliminary drainage by means of passing a ureteral catheter by the obstructing calculus in the ureter. If the stone is tightly impacted or embedded in the ureter it is sometimes impossible to pass even in spite of placing the patient in the exaggerated Trendelenburg position and in spite of maneuvering filiforms, bougies, and catheters of all description and angles. The catheter should be left in place. It assures drainage of urine and acts as a guide for the location of the stone when surgical intervention is made. It is of particular aid when perireteritis or huge dilatation of the ureter has rendered its palpation or visualization difficult. If the stone is located low down in the ureter its removal can be greatly facilitated by making an incision above the stone and extracting it by the aid of a small forceps (Fig. 5). In some cases the stone can be milked up into the incision where it is readily removed. The incision in the healthy portion of the ureter well above the site of the stone, where it often has caused more or less ureteritis and perireteritis, assures better healing and is more likely to eliminate the possibility of subsequent stricture formation. It is well not to close the ureter by suture but to leave it wide open to assure sufficient drainage. After the stone has been removed one should make sure that the ureter is replaced in its proper place eliminating the possibility of forming an abnormal angulation which would later impede the outflow of urine.

## SUMMARY

1. The management of stone in the solitary kidney and ureter includes many prophylactic measures, viz.: the early removal of unilateral calculi and nephrectomy for calculus pyonephrosis which might act as a focus for stone formation in its healthy fellow; the clearing up of all foci of infection in other portions of the body; the elimination of stasis in the upper and lower urinary tract; the eradication of infection in the remaining kidney, and a careful regimen and limitation of diet and abstinence of excesses in eating and drinking.

2. Five cases are reported, the clinical cause of which emphasize the early removal of stone from the solitary kidney before renal insufficiency and advanced infection have set in often transforming a good subject for surgical relief into a hazardous risk. When performed, early lithotomy on the solitary kidney and ureter is a benign operation followed by practically no shock and tolerated as well as by patients possessing two kidneys.

3. Attempts to cause stones to pass from the solitary kidney pelvis or ureter by cystoscopic maneuvers are dangerous because the stone, in passing, is likely to obstruct the ureter. In cases presenting chronic pyelonephritis this obstruction is likely to cause invasion of the parenchyma by the infecting organisms present, resulting in destruction of the kidney, anuria, uræmia, and death.

4. Surgical removal of stone from the solitary kidney and ureter calls for the most exacting operative technique and keen surgical judgment. Preliminary drainage and lavage should be made through the ureteral catheter. A wide incision assuring good exposure should be made, extreme gentleness should be employed in handling the kidney, blood vessels should not be sacrificed, and the incision in the pelvis and ureter should not be sutured in order to assure drainage. A combination pyelotomy and nephrotomy incision assures entire removal of the stone and is less likely to be followed by recurrence. Decapsulation should be made to avoid postoperative renal congestion.

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# THE CONSERVATIVE TREATMENT OF PREPATELLAR BURSITIS[1]

## A Study of Twenty-Seven Consecutive Cases with Follow-Up Results

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THE common affections of the prepatellar bursa are those due to acute inflammation with or without suppuration, chronic simple inflammation, tuberculosis, or syphilis. This paper is concerned with both acute and chronic inflammations ("house-maid's knee") producing a painful or non-painful swelling without calcification and with fluid of a non-purulent character present.

The opinions of various men as to the treatment of this condition are of interest. Jones and Lovett state: "If from the patient's neglect or other causes the condition becomes chronic, the bursa should be dissected out." Telford says: "For the larger and older cases the extirpation of the sac is the only possible treatment; aspiration and injection are futile and may be dangerous." Reder advised incision and drainage of non-suppurative prepatellar bursitis but in chronic cases complete excision of the bursa. Hoffman, among others, advocated puncture of the bursa, expression of its contents, scarification of its walls, and firm bandage pressure. He had 104 cases. In 2 cases, this procedure was carried out twice; in 4 cases three times; while in 98 cases it was successful after one treatment. The length of the follow-up is not given. Field and Allen report traumatic subcutaneous rupture of the prepatellar inflamed bursa. In Field's case the swelling was not in evidence 6 months later. Among those who have reported a few cases treated by aspiration, or aspiration and injection of a chemical irritant, are Heath, Morse, and Favardin. No late follow-up results are given.

Maingot records the excision of a partially calcified prepatellar bursa of 30 years' duration in a woman of 56. It measured 11½ by 9¾ inches and weighed 63 ounces.

In 24 of 27 consecutive cases of non-suppurative prepatellar bursitis treated in the out-patient-department of the Presbyterian Hospital, successful end-results were obtained without operative therapy. In the 3 remaining cases there was no follow-up.

The technique employed is simple. A needle of sufficient caliber attached to a 20 cubic centimeter syringe is inserted, without an anæsthetic, into the bursal cavity. The fluid is evacuated as completely as possible and then from 2 to 5 cubic centimeters of half strength, 3.5 per cent, tincture of iodine is injected into the bursa. The needle is withdrawn and the skin of the bursa massaged vigorously in order to disseminate the iodine in the bursal sac. The patient may now feel a burning pain. The knee is placed in complete extension

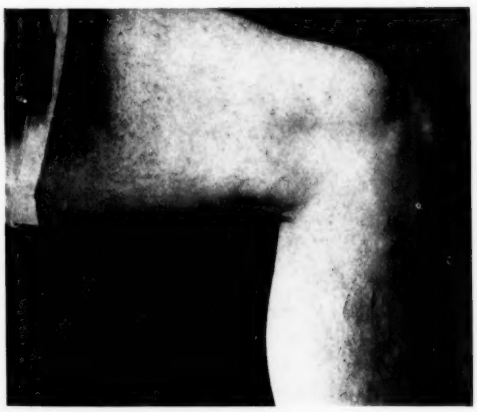

Fig. 1. Lateral view of knee of a 21 year old male (Case No. 123008) who had a traumatic prepatellar bursitis of 7 weeks' duration.

Fig. 2. Photograph of bursa excised in case in Figure 1, after bisection. There is a pale, smooth, fibrous lining. Scattered over the surface of this are many elevated, dark reddish papillary projections from 1 to 3 millimeters in diameter. From one of these a slender thread of tissue passes from one side of the sac to another. (Courtesy of Dr. A. P. Stout.)

[1]From the Presbyterian Hospital, College of Physicians and Surgeons, Columbia University.

TABLE I.—TWENTY-SEVEN CASES OF PREPATELLAR BURSITIS TREATED BY AUTHOR'S METHOD

| Case No. Date | Age Sex | Occupation | Trauma | ide | Symptoms | Signs | †Amount and character of fluid aspirated | Culture | Amount of chemical injected | Course after treatment | *Result |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 2743 1-○-21 | 47 F | Housewife | Fell on knee | Right | Discomfort in walking. Immediate swelling | Swelling in which is crepitation | 12 c.cm. bloody fluid | Negative | 1 c.cm. 5% iodine | 1 week small amount fluid, no symptoms. 3 weeks, well | 5 years, well |
| 12562 3-22-22 | ?2 F | None | Prays on knees | Right | Swelling | Size of egg | 25 c.cm. amber fluid | | 3 c.cm. 3.5% iodine | Pain for 2 days, no fluid; 5 days no pain nor fluid; 3 weeks small amount fluid | 2 years, well |
| 110102 12-26-22 | 53 F | Housewife | Struck knee | Right | Swelling in 24 hours | Swelling | 20 c.cm. reddish brown fluid | | 5 c.cm. 3.5% iodine | 2 days, no pain nor swelling; 3 weeks well | 3 years, well |
| 92699 10-15-10 | 50 F | Housewife | Fell on knee | Right | Pain and tenderness; swelling 6 months later | Swelling, non-inflammatory and non-tender | | | 1 c.cm. 7% iodine | 9 days, reaspiration 15 c.cm. fluid. Injection of 10 drops pure carbolic; 10 days well | 6 years, well |
| 138349 8-10-25 | 42 F | Housewife | Scrubs on knees | Left | Swelling (several weeks) | Fluid in bursa | 10 c.cm. straw-colored fluid | Negative | 2.5 c.cm. 3.5% iodine | 1 week, no fluid; 2 weeks, well | 3 years, well |
| 87345 4-23-19 | 53 F | Housewife | Kneels | Right | Slightly painful swelling (3 months) | Swelling 4 x 4 cm. slightly tender and fluctuant | 4 c.cm. clear yellow fluid | Negative | 1 c.cm. 3.5% iodine | 16 days 8 c.cm. fluid aspirated | 9 years, no swelling nor symptoms |
| 156576 3- 3-27 | 40 F | Cook | Fell on knee | Right | Painful swelling | Fluctuant tender swelling | 30 c.cm. thin bloody fluid | Negative | None, at first | 6 days, fluid reaccumulated, 20 c.cm. bloody fluid aspirated; 1 c.cm. 3.5% iodine injected 9 days, well | 14 months, well |
| 157948 4- 4-27 | 15 M | Student | Fell on knee | Left | Immediate pain; swelling 2 weeks later. Present 4 weeks | Fluctuant swelling | 10 c.cm. bloody fluid | Negative | 3 c.cm. 3.5% iodine | 3 days, little fluid present; 9 weeks slight fluid, well | 13 months well |
| 161184 6- 8-27 | 16 F | Student | Fell on knee 6 months ago | Left | Swelling | Fluctuant swelling | 3 c.cm. fluid | | 1 c.cm. 3.5% iodine | 6 months fluid persisted, 45 c.cm. clear straw-colored fluid aspirated; 6½ months 3 c.cm. 3.5% iodine injected; 7 mo. some swelling | 1 year well; 2 x 2 cm. thickening in region of bursa |
| 166573 12-22-27 | 52 M | Fireman | | Right | Swelling 2 days | Swelling 4 x 5 cm. fluctuant, slightly tender | 40 c.cm. clear, bloody fluid | Negative | None at first | 16 days reaspiration 24 c.cm. bloody fluid injection of 2 c.cm. 3.5% iodine; 3 days slight tenderness; 8 days slight swelling | 4 months no swelling nor pain |
| 5153 2- 3-23 | 33 M | Carpenter | | Right | Non-painful swelling | Swelling 4 x 7 cm. | 8 c.cm. opaque, yellowish fluid | Negative | 3 c.cm. 3.5% iodine | 1 week no symptoms nor fluid | 3 months, well |
| 103051 9-28-20 | 30 F | Housewife | Bruise | Right | Swelling appeared in 3 months | Cystic swelling | | | | | 9 weeks, well |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 89555<br>10–14–19 | 43<br>F | Cleaner | Fell on knee | Right | 2 months later swelling—1 month | Prepatellar bursa, tense no redness nor tenderness | | | Tincture of iodine | 2 weeks slight return fluid; 4 weeks well | 4 weeks, well |
| 76152<br>1– 9–19 | 64<br>F | Housewife | | Right | Swelling for 1 month | Swelling | 6 c.cm. bloody fluid | | 2 c.cm. 3.5% iodine | | 3 weeks, well |
| 90867<br>8–16–19 | 53<br>F | Cleaner | On knees while cleaning | Right | Lump for 4 years | Swelling 7.5 cm. in diameter | 50 c.cm. thin bloody fluid | Negative | 10 drops pure carbolic | 3 weeks no fluid | 4 weeks, well |
| 95212<br>9–28–20 | 57<br>F | Housewife | | Right | Swelling | Swelling size of mandarin orange | | | 2 c.cm. 3.5% iodine | 1 week, slight reaccumulation fluid | 3 weeks, slight amount fluid in bursa |
| 94387<br>12– 8–19 | 25<br>F | Housewife | Fell on knee | Left | Pain and soreness several days. Swelling 2 months later | Swelling 2.5 x 3 cm. Skin purplish | 30 c.cm. bloody fluid | | 10 drops 10% iodine | 2 weeks, well | |
| 12004<br>10–15–21 | 25<br>F | Waitress | Fell on knee | Right | Swelling 1 week later | Swelling 3 x 3 cm. Fibrinous plaques felt | 12 c.cm. bloody fluid | | 2 c.cm. 3.5% iodine | 2 days, small amount of fluid; 6 days aspiration 3 c.cm. brownish fluid | 5 weeks, well |
| 85153<br>2–26–19 | 46<br>F | Cook | Kneels | Right | Swelling | Swelling | 8 c.cm. fluid | | 1 c.cm. 3.5% iodine | 6 weeks, reaccumulation of fluid | |
| 106806<br>9–13–22 | 33<br>F | Housewife | Struck knee | Right | Immediate swelling | Swelling 5 x 5 cm. | 14 c.cm. turbid bloody fluid | | 3 c.cm. 3.5% iodine | 2 days, pain, small amount of fluid; 1 week, small amount of fluid | |
| 114266<br>5–23–23 | 17<br>F | Chambermaid | | Right | Swelling 3 months | Swelling 6 x 5 cm. | 15 c.cm. clear yellow fluid | | 3 c.cm. 3.5% iodine | 1 week, 5 c.cm. fluid aspirated; 9 days, 3 c.cm. fluid aspirated | |
| 155243<br>1–12–27 | 30<br>F | Housewife | | Right | Painful swelling 6 weeks | Swelling 8 x 8 cm. fluctuant | 20 c.cm. bloody fluid | Negative | 1 c.cm. 3.5% iodine | 2 days, fluid present, aspirated; 5 days, 5 c.cm. serosanguineous fluid | 2 weeks, well |
| 149632<br>6–14–26 | 26<br>F | Housewife | | Right | Pain and swelling 4 weeks | Swelling 7 x 6 cm. fluctuant | Aspirated | | 1% iodine | 5 days, no swelling; 12 days, slight swelling, well | |
| 148781<br>5–21–26 | 59<br>M | Lumber | Fell on knee | Left | Swelling (several days) | Large swelling | 35 c.cm. bloody chocolate fluid | Negative | 5 c.cm. 3.5% iodine | 2 days, fluid in bursa; 4 days, less fluid; 6 days 30 c.cm. reddish fluid aspirated; 8 days, some swelling | |
| 85793<br>3– 4–19 | 32<br>F | Housewife | | Left | Painful swelling 3 weeks | Swelling | 12 c.cm. fluid | | 1 c.cm. 7% iodine | | |
| 75986<br>1–31–18 | 22<br>M | Painter | Struck knee | Left | Swelling | Swelling | 50 c.cm. light yellow fluid | | 3.5% iodine | | |
| 67261<br>3–13–17 | 38<br>M | Steward | Fell on knee | Right | Painful swelling | Swelling | 15 c.cm. clear amber fluid | Negative | 1/200 phenol | | |

†Kling (11) found that the bursal fluid occasionally had the character of a transudate with a specific gravity of about 1010 and with relatively few cells. The icteric index was between 2 and 5 in the transudates, gelatinous and inflammatory fluids. Hæmorrhagic fluids gave a high icteric index, between 10 and 30.

*Some of these follow-up results were not seen by the writer but while being treated in other departments in the hospital the patients made no complaints about the bursitis.

TABLE II.—ANALYSIS OF TWENTY-SEVEN CASES OF PREPATELLAR BURSITIS

Age in years

| | |
|---|---|
| Oldest | 72 |
| Youngest | 15 |
| Average age | 40.6 |

Sex

| | Cases | Per cent |
|---|---|---|
| Males | 5 | 19 |
| Females | 22 | 81 |

Occupation (in order of frequency)

| | Cases | Per cent |
|---|---|---|
| 1. Housewife | 14 | 53 |
| 2. Cook | 2 | 7 |
| Cleaner | 2 | 7 |
| Student | 2 | 7 |
| 3. Miscellaneous | 7 | 26 |

Trauma

| | Cases | Per cent |
|---|---|---|
| Positive | 18 | 67 |
| Negative | 0 | 0 |
| Not recorded | 9 | 33 |

Duration—20 cases

In five cases (25 per cent) the swelling appeared immediately. In the 15 remaining cases it appeared in days, weeks, or months. At time of first observation the shortest time for appearance of swelling was immediately; the longest 4 years (1 case); average, 1½ months (excluding the 4 year case).

Analysis chief complaints

| | Cases | Per cent |
|---|---|---|
| 1. Swelling | 21 | 68 |
| 2. Pain | 8 | 26 |
| 3. Discomfort on walking | 1 | 3 |
| 4. Tenderness | 1 | 3 |

Analysis of objective symptoms

| | Cases | Per cent |
|---|---|---|
| 1. Swelling | 27 | 100[1] |
| 2. Fluctuation | 7 | 26 |
| 3. Tenderness | 3 | 11 |
| 4. Discoloration of skin | 1 | 4 |
| 5. Crepitation | 2 | 8 |

[1](Largest swelling, 12 by 12 cm.; Smallest swelling, 3 by 3 cm.; Average size, 6 by 6 cm.)

and an attempt is made to coaptate the walls of the sac by firm and reinforced adhesive strapping. A pressure bandage is then applied over the knee so that the patient must walk with the knee in complete extension. Usually the patient has very little discomfort from these procedures. In about half the cases the dressings can be removed in from 5 to 7 days without further treatment. In the remaining cases there is reaccumulation of fluid in a few days to such an extent that reaspiration is necessary in about half of them. The strapping and the pressure bandage are continued. A second injection of tincture of iodine is usually not necessary.

Aspirated fluid[2]

| | Cases | Per cent |
|---|---|---|
| A. Character: | | |
| Bloody | 11 | 64 |
| Yellow | 5 | 24 |
| Amber | 2 | 8 |
| Red brown | 1 | 4 |
| Not recorded | 8 | 29 |
| B. Culture of aspirated fluid: | | |
| | 11 negative | |

[2](Largest amount, 50 c.cm.; Smallest amount, 3 c.cm.; Average amount, 19.5 c.cm.)

Treatment

| | Cases | Per cent |
|---|---|---|
| a. Iodine injected | 25 | 90 |
| Average amount 4.5 c.cm. | | |
| Average strength 3.5 per cent | | |
| b. Injection: pure carbolic | 1 | 5 |
| 10 minims. | | |
| c. Injection: phenol 1:200 | 1 | 5 |

Course after treatment

| | Cases | Per cent |
|---|---|---|
| a. Number of cases in which fluid reaccumulated | 16 | 60 |
| b. Length of time after first aspiration. Longest, 42 days; shortest, 2 days; average, 10.4 days. | | |
| c. Type of fluid: | | |
| Not known or not recorded | 10 | 63 |
| Red (serosanguineous) | 4 | 25 |
| Brown | 1 | 6 |
| Straw | 1 | 6 |

Treatment of reaccumulated fluid

| | Cases | Per cent |
|---|---|---|
| Aspiration | 5 | 31 |
| Aspiration plus iodine (3½ per cent) | 3 | 19 |
| Aspiration plus carbolic (pure—10 drops) | 1 | 6 |
| No treatment | 7 | 44 |
| Total number of cases in analysis | 27 | |
| Total number of follow-up cases | 24 | |
| a. Follow-up time: | | |
| Shortest follow-up | (¼ month) 7 days | |
| Longest follow-up | 108 months | |
| Average follow-up | 16.3 months | |

Although a satisfactory end-result might have been obtained in some of these cases without any treatment, the eventual complete disappearance of bursal fluid and of symptoms seems to justify the therapy as described.

SUMMARY

1. Twenty-seven consecutive acute or chronic cases of prepatellar bursitis ("house-maid's knee") were studied to determine the end-results of conservative therapy. This consisted in aspiration of the fluid, injection of several cubic centimeters of half strength tincture of iodine into the sac, vigorous massage over the bursa, reinforced adhesive strapping over the sac with the knee in complete extension, and the application of a firm pressure bandage over the knee.

2. The cases were preponderant in housewives.

Fig. 3. Low power photomicrograph through one of the red papillary projections shown in Figure 2. The wall is dense and fibrous. The projection stands out because of the presence of a large number of capillaries surrounded by a more cellular fibrous tissue. (Courtesy of Dr. A. P. Stout.)

3. About 65 per cent of the patients gave a history of trauma.

4. About one-third of the cases complained of pain.

5. Swelling of the bursa appeared either immediately after the trauma or after days, weeks, or months.

6. The character of the aspirated fluid depended on the length of time it took for accumulation. In the early cases it was bloody; in the later cases amber or straw-colored.

7. Aerobic and anaerobic cultures in 11 cases were sterile.

8. In a little more than half the cases small amounts of fluid reaccumulated in an average time of 10 days. Aspiration of this fluid was employed. A second injection of tincture of iodine in these cases was usually not necessary.

9. An average follow-up of 16 months in 24 out of the 27 cases showed no symptoms or reappearance of bursal fluid. In 20 of the 24 follow-up cases the average time for complete disappearance of the fluid was about 3 weeks.

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# BILIARY TRACT VISUALIZATION WITH RADIOPAQUE OILS[1]

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THE use of radiopaque solutions to define the biliary ducts after a drainage operation has proved of sufficient value during the past year to warrant the publication of the results of such a procedure.

The value of exact information concerning the size, contour, and the patency of the cystic or common duct following cholecystectomy or of the common and hepatic ducts following choledochostomy need not be emphasized. Following such operations, there is frequently an uncertainty about underlying pathology, overlooked stones, or the extent of trauma to the biliary ducts. The more limited the exploration at the time of operation the greater this uncertainty.

A definite knowledge of the patency of the biliary duct system is required in the proper postoperative management of the case, such as the determination of the time for withdrawal of the T-tube, and in giving a prognosis as to the probability of a persisting biliary fistula. The determination of obstruction of the common duct before the T-tube is withdrawn is also important if a second operation is required, as the common duct is more easily located if the T-tube is left *in situ*.

There are various indirect ways of gaining information about the condition of the common biliary duct after operation. The measurement of the external drainage during a given period of time and its subtraction from the estimated total biliary output indicates the amount of the internal drainage. Macroscopic and chemical examination of the stools for bile pigment, as well as the disappearance of jaundice, and the improvement in the Van den Bergh reaction, all are used to determine common duct patency. The ability to clamp the T-tube without causing discomfort, an increase in jaundice or in the Van den Bergh reaction, or a leak about the tube in the wound is generally taken as sufficient indirect evidence to say that the common duct is patent.

However, in some patients these criteria are not reliable. Especially is this true in patients in whom there has been some hepatic drainage with a suppression of biliary output. The external drainage may be small, the stools light, and the jaundice slow in clearing, yet the common duct may be patent. On the other hand, indirect evidence may readily suggest that there are present a normally functioning ampulla and a partial occlusion.

On the service of Dr. George P. Muller, we have found that in a certain number of postoperative biliary cases, a roentgenological study during the injection of a radiopaque solution is of distinct value. Twelve such examinations upon eleven different patients were made.

Lipiodol injections of chronic biliary fistulæ have been carried out and the diagnostic importance of such a procedure pointed out by Piccinico and Pazienza, Caeiro, and by Ginzburg and Benjamin. There are fewer reports of the use of such a procedure in securing information about a case after operation before the T-tube has been removed. Cotte, however, has emphasized the value of the visualization of the biliary tract with the T-tube in place.

## METHOD

During the second or third week after operation, the patient is placed on an adjustable fluoroscopic table. The gall-bladder drainage tube or common duct tube is then injected with the opaque material, under fluoroscopic control, the amount varying from 15 to 20 cubic centimeters, depending upon the manner in which the biliary system fills. No force is required to make the injection as the solution will practically run into the ducts by the force of gravity.

We found campiodol (iodized rape seed oil) to be a safe and satisfactory visualizing medium. This substance was introduced by Frazier and Glaser for use in cerebrospinal visualization. Later, Frazier pointed out the advantages of campiodol for general use in roentgenological exploration. In a few patients we used brominol, a brominized olive oil. Satisfactory visualization was obtained without evidence of tissue irritation. Brominol has the advantage of being less expensive than the other radiopaque oils. Sodium iodide was tried, but the flow of this solution was more difficult to follow fluoroscopically.

When a complete or partial obstruction of the common duct was noted, the drainage tube was clamped following the injection and fluoroscopic examinations made at intervals over a period of 30 to 40 minutes. In some a duodenal tube was passed, and a solution of magnesium sulphate was injected.

[1] Read before the Surgical Research Society, Philadelphia, March 15, 1930.

Fig. 1. Roentgenogram made 3 weeks after cholecystectomy and choledochostomy. Note visualization of hepatic ducts which show marked dilatation. No campiodol seen in duodenum. Obstruction at ampulla complete. *C*, Common duct; *T*, drainage tube; *H*, hepatic ducts; *R*, Rehfuss tube in first portion of duodenum.

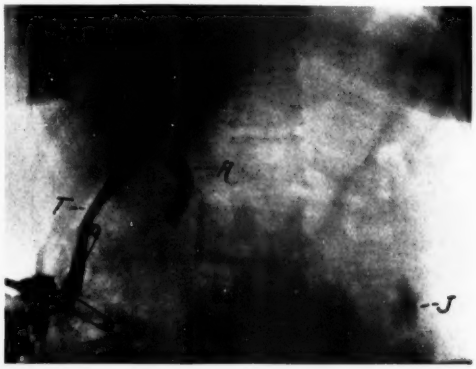



Fig. 2. Roentgenogram made one week after choledochostomy. Duct system well visualized. Note that small amount of campiodol escaped into the gall bladder fossa at the base of the liver. Only an occasional drop of oil passed into the duodenum. This can be seen in the jejunum on the opposite side of the roentgenogram. *T*, Drainage tube; *A*, common duct; *H*, hepatic ducts; *J*, campiodol in proximal jejunum.

In no instance was there an untoward result following the injection of the biliary system.[1] Mallet-Guy, Beaufere, and Armanet are the sole ones to report a complication. They injected lipiodal and repeated the injection two different times in order to get a visualization of the ducts. The introduction of the lipiodal was not fluoroscopically controlled.

## RESULTS

In the patients in whom no obstruction to the emptying of the common duct existed, the campiodol passed immediately through the duct and into the duodenum. At times the flow of the oil would be checked at the ampulla momentarily, during which interval, waves in the common duct seemed to sweep the oil toward the hepatic ducts, before it would enter the duodenum. In such cases, however, the hepatic ducts filled poorly and the common duct incompletely (Figs. 3 and 5). Roentgenograms showed the opaque medium scattered in the upper jejunum. It is well, for this reason, to make a large enough exposure to include both upper quadrants of the abdomen.

When an obstruction existed in the common duct, this duct as well as the hepatic ducts promptly filled and were clearly visualized (Figs. 1, 2, and 4). The position, contour, and size of these ducts were clearly determined. Incomplete common duct obstruction in some cases was evidenced by a filling of the duct system with only small expulsions of oil into the duodenum. When contraction waves were seen in the common duct, with obstruction present, there was a tendency for the opaque medium to be forced higher in the hepatic ducts.

The injection of a cholecystostomy drain with obstruction of the common duct showed the gall bladder, cystic and hepatic ducts (Figs. 6 and 7). If there was no obstruction, the gall bladder and ducts filled poorly and immediate entrance of the campiodol into the duodenum was noted (Fig. 8). This information was especially important as it was in such cases that exploration at the time of operation was unwise.

During the course of the roentgenological exploration of the biliary system in one case we were able to observe actual rhythmic contractions of the gall bladder, which continued after the patient was asked to stop breathing (Fig. 6). In another patient the tortuosity of the cystic duct due to the valves of Heister was beautifully outlined (Fig. 8).

In cases in which the common duct obstruction had existed for a long period of time, a dilatation of the hepatic ducts could be demonstrated. In our cases the degree of hepatic duct dilation corresponded closely to the degree of liver drainage as estimated by the biliary output, the change in

[1] In one patient nausea and vomiting followed 18 hours after campiodol was injected into the biliary system. Through error the T-tube had been left clamped with an obstructed common duct. Symptoms disappeared after the T-tube was opened.

Fig. 3. Appearance when common duct is patent. Roentgenogram made 2 weeks after cholecystectomy and choledochostomy. Note poor visualization of hepatic ducts and the presence of most of the campiodol in the jejunum. *T*, Drainage tube; *H*, hepatic ducts; *D*, campiodol in duodenum; *J*, campiodol in jejunum.

Fig. 4. Roentgenogram made 2½ weeks after cholecystectomy and choledochostomy. Note dilatation of biliary ducts with obstruction at ampulla. Only an occasional drop of campiodol passed into the duodenum. *T*, Drainage tube; *H*, dilated hepatic ducts; *A*, obstructed ampulla.

the Van den Bergh reaction, and the duration of the convalescence.

Case 8. Mr. J. E. P., aged 33 years, admitted to hospital December 30, 1929 (Fig. 1). There were symptoms of gall-bladder disease of 2 months' and jaundice of 1 month's duration. After a 4 day preparation, patient was operated upon by Dr. G. P. Muller. A subacute cholecystitis was found. A cholecystectomy and choledochostomy were done. Several drams of gravel were removed from the dilated common duct. Following operation, the jaundice disappeared very slowly. Three weeks after operation a Van den Bergh test showed a biphasic direct reaction and 1.6 units by the indirect test. Drainage from the common duct tube varied from 450 cubic centimeters to 1,010 cubic centimeters for each 24 hours. The stools were light in color for 2 weeks, then became darker, and bile pigment could be found in the fæces. Clamping the common duct tube was tolerated fairly well by the patient, although epigastric distress occurred at times.

Three weeks after operation, campiodol was slowly injected into the common duct with the patient under the fluoroscope. The opaque medium entered the common duct and hepatic ducts immediately. These ducts were dilated. None of the oil entered the duodenum. Frequent peristaltic waves in the common duct forced the oil farther up the hepatic ducts. The tip of the Rehfuss tube previously passed was found in the stomach and attempts to have the tube enter the duodenum failed. Fifty cubic centimeters of a 50 per cent solution of magnesium sulphate was injected into the Rehfuss tube, however, and no effect on the oil in the common duct was noted. The patient was under observation for a period lasting 40 minutes. The patient was discharged and requested to return to the follow-up clinic every 2 weeks, operation to be advised if patency of the common duct did not re-establish itself in a reasonable period of time.

In this patient the injection of oil into the common duct established definitely the fact that an obstruction still existed. The removal of the common duct T-tube was advised against as a biliary fistula would certainly follow and the drainage be less conveniently handled. The dilated hepatic ducts were an additional factor in this case which suggested marked liver damage due to prolonged ductal obstruction.

Case 2. Mrs. R. B., aged 36 years, admitted to hospital August 30, 1929 (Fig. 2). A history referable to gall-bladder disease antedated the patient's admission by 13 months. A cholecystectomy had been done 5 months previously. Attacks of pain reappeared 3 months ago and were associated with jaundice. The physical examination revealed nothing unusual except those findings associated with the common duct obstruction. The Van den Bergh reaction showed a direct biphasic and an indirect test of 12 units. The icteric index was 100. After the usual preparation, the patient was operated upon by Dr. Muller and an obstruction of the common duct due to a cicatrix was found about 3 centimeters above the ampulla. No stones were located. A T-tube was inserted.

Convalescence was quite uneventful. Drainage from the T-tube varied from 600 to 1,200 cubic centimeters daily and the jaundice decreased slowly. Nine days after operation the common duct tube was injected with campiodol under fluoroscopic visualization. The oil went into the duodenum rather sluggishly, and the common and hepatic ducts filled fairly well.

The amount of drainage continued to be 600 to 700 cubic centimeters for each 24 hour period. Continual clamping of the common duct tube caused some distress. For these reasons and because the emptying of the common duct was sluggish as visualized roentgenoscopically, the T-tube was left *in situ*, and the patient was advised that it could be removed in 6 weeks. This was done and the sinus closed rapidly.

In this case, roentgenoscopic visualization of the biliary system substantiated the indirect evidence that a free flow of bile into the duodenum

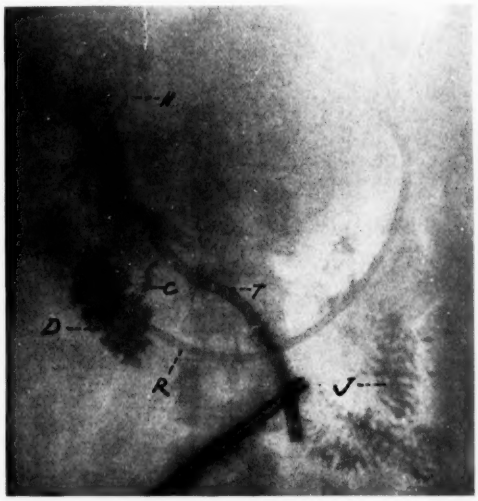



Fig. 5. Biliary tract injected with campiodol 7 days after operation. Note poor visualization of hepatic or common ducts. The oil went almost immediately into the duodenum where a large portion of it can be seen. The relation of the common duct to the duodenum is clearly seen. Note that some of the campiodol is in the jejunum. *H*, Hepatic ducts; *C*, common duct; *D*, campiodol in duodenum; *T*, drainage tube; *J*, oil in jejunum; *R*, jutte tube in duodenum.

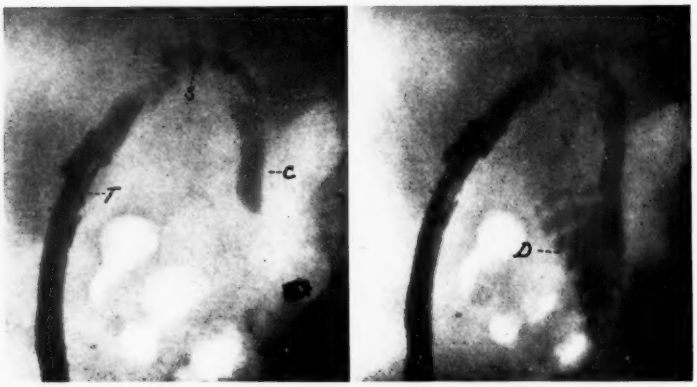
Fig. 6. Roentgenogram made after cholecystostomy drainage tube had been injected with 20 cubic centimeters campiodol. The gall bladder and right hepatic ducts are well visualized. No trace of oil can be seen in upper intestinal tract. *H*, Hepatic ducts; *G-B*, gall bladder; *T*, drainage tube.

was not taking place. For this reason withdrawal of the T-tube in the common duct was delayed.

Case 7. Mrs. R. E. G., aged 59 years, was admitted to hospital March 1, 1930 (Fig. 4). She had been seriously ill for a week with chills, fever, jaundice, and pain in the upper right quadrant. A diagnosis of acute cholecystitis was made and operation was delayed for 5 days until a subsidence of symptoms occurred. A cholecystectomy and choledochostomy were done. The general condition of the patient improved, the jaundice cleared slowly, the Van den Bergh values decreased, and occasionally the stools were dark in color. The external drainage varied from 100 to 400 cubic centimeters in a 24 hour period. Two and one-half weeks after operation the T-tube was injected with 20 cubic centimeters campiodol under the fluoroscope. The oil immediately filled the common and hepatic ducts. Only an occasional drop could be seen passing into the duodenum. The hepatic ducts were greatly dilated. The patient was later discharged with the T-tube in place. She returned after 2 months. The biliary tract was again visualized roentgenoscopically. The same dilated hepatic and common ducts with almost complete obstruction at the ampulla were found. Re-operation was recommended and choledochoduodenostomy was carried out with the T-tube still in place until the common duct was isolated. The patient made an uneventful recovery.

In this case a definite obstruction at the ampulla was determined early, the drainage tube left in place, and the external drainage conveniently handled until a second operation could be

Fig. 7. Roentgenogram made after campiodol was injected in a cholecystostomy drain. This patient had an acute cholecystitis. Exploration was impossible. The injection demonstrated complete common duct obstruction. One of the drainage tubes is beneath the gall bladder. *H*, Hepatic ducts; *G-B*, gall bladder; *C*, common duct; *T*, drainage tubes.




A. B.

Fig. 8. Roentgenograms made after brominal injection of cholecystostomy drain, *T*. This patient had an acute cholecystitis and pancreatitis. No obstruction found. Note spiral appearance of cystic duct, *S*. Common duct, *C*, is well visualized. A, Before ampulla opened; B, during flow of oil into duodenum, *D*.

safely performed. The early withdrawal of the T-tube would have made the location of the common duct more difficult at the second operation.

CASE 5. Mr. J. McK., aged 55 years, was admitted to hospital September 23, 1929 (Fig. 5). The history referable to gall-bladder disease dated back 8 months. Following a severe attack of upper right quadrant pain 6 weeks previously, the patient had become jaundiced. There was nothing unusual in the physical examination or laboratory tests other than those associated with a deep jaundice. At operation, Dr. Muller found a cicatricial stenosis of the common duct, but no stones were present here or in a subacutely inflamed gall bladder. A cholecystectomy was done and the common duct drained. Convalescence was uneventful. The amount of biliary drainage averaged 100 cubic centimeters in each 24 hour period. The jaundice rapidly disappeared. Seven days after operation the common duct was injected with campiodol under the fluoroscope. The opaque oil went into the duodenum from the common duct. The remainder of the convalescence was uneventful. On the sixteenth day after operation the T-tube was removed and the biliary fistula quickly closed.

In this case the drainage was very slight, the jaundice cleared rapidly and the stools assumed a normal color early in the convalescence. All of these factors indicated a patent common duct. The direct visualization of the ducts substantiated the indirect evidence of common duct patency.

CASE 4. Mrs. M. M., aged 43 years, was admitted to the hospital July 6, 1929 (Fig. 6). This patient had had epigastric distress and nausea for 8 months. Jaundice appeared 1 month before she entered the hospital and was progressively increased in severity. After a 4 day period of preparation, the patient was operated upon by Dr. George P. Muller. A carcinoma of the head of the pancreas was found. Only cholecystostomy was done because of the poor condition of the patient and technical difficulties in mobilizing with the stomach or duodenum for anastomosis. Following operation the jaundice cleared very slowly, the drainage varied from 100 to 400 cubic centimeters for each 24 hour period, and the stools remained a putty color. Four weeks after operation, campiodol was injected into the gall bladder via the drainage tube. Under the fluoroscope rhythmic contractions of the gall bladder could be seen. These were not influenced by the respiratory movements and were present when the patient held her breath. The opaque oil passed into the common duct and was regurgitated up into the hepatic ducts. Occasionally drops of oil could be seen passing through the ampulla and into the duodenum. The patient's general condition failed to improve enough to warrant completing the second stage of the operation. She was discharged with the tube *in situ* and died 5 months later after a rapid extension of the carcinoma.

From the standpoint of gaining information which could be applied in the management of this case, little was obtained by the use of the opaque injection. However, we were able to see rhythmic contractions of the human gall bladder which have never before been demonstrated.[1]

CASE 11. Mrs. M. McG., aged 61 years, was admitted to the hospital February 2, 1930 (Fig. 8). This patient had had symptoms referable to the gall bladder for 5 months and during the past 2 months jaundice was associated with the attacks of pain in the right upper quadrant. The patient was treated in the medical ward for 12 days and was then transferred for surgery. At operation, Dr. G. P. Muller found an acute calculous cholecystitis and an acute pancreatitis. Further exploration was decided against and a cholecystostomy was done. Convalescence was uneventful. The jaundice subsided rapidly. Drainage from the gall bladder amounted to 500 cubic centimeters the first 24 hours and then decreased to about 100 cubic centimeters in each 24 hours. Two weeks after operation, campiodol was

[1] This fluoroscopic observation was made in the presence of Dr. I. S. Ravdin and Dr. E. P. Pendergrass. See I. S. Ravdin's "Observations on the Contractions of the Gall Bladder." Ann. Surg., to be published.

injected into the gall bladder via the drainage tube. The opaque media passed immediately through a tortuous cystic duct into the common duct, which filled completely. No defects in the contour of the common duct were noted, and periodically the ampulla opened and the opaque solution passed rapidly into the duodenum. On the day following this test of the patency of the common duct, the tube within the gall bladder was removed, the fistula closed, and the wound healed. The patient was discharged on the twentieth day after operation.

In this case it was impossible and unwise to palpate or open the common duct, yet there was a history of jaundice. The injection of an opaque solution into the biliary system showed definitely the absence of stones in the cystic or common duct and a patent ampulla. With such information we were able to remove the drainage tube immediately and to advise the patient that a biliary fistula would not result.

## SUMMARY

The use of a radiopaque oil for roentgenoscopic exploration after biliary tract operations has a definite value in the determination of common duct patency. No untoward effects following such a procedure were noted.

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# OVARIAN PREGNANCY

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OVARIAN pregnancy was first described in the 17th century, by Mercerus and St. Meurice, and its possibility was generally conceded until 1835, when Velpeau stated that none of the cases which had been described up to that time afforded conclusive evidence of ovarian origin. Similar views were expressed by Mayer in 1847. This skepticism was probably justifiable, since most of the early cases collected were simply dermoid cysts of the ovary.

With the exception of Mayer, the possibility of ovarian pregnancy has always been admitted by the German writers, but was strenuously denied until 1901 by the English authorities, particularly by Tait, Webster, and Bland-Sutton.

Williams states that as far as he can ascertain, only 3 cases were reported in England during the 19th century. In this country most writers have followed the English authorities, although Parry admitted its existence and not a few operators had reported doubtful cases; but it was not until 1902 that Thompson demonstrated a conclusive specimen.

Up to 1878 there existed no definite criteria by which specimens could be judged, and many were described as examples of ovarian pregnancy which had no claim to such a title. In that year, however, Spiegelberg formulated certain criteria which he held must be fulfilled in order to justify such a diagnosis. He demanded (1) that the tube on the affected side be intact; (2) that the fetal sac occupy the position of the ovary; (3) that it be connected with the uterus by the ovarian ligament; (4) that definite ovarian tissue be found in its wall. When judged by these criteria, the majority of cases which had been described up to his time were wanting, and subsequent investigation has shown that a number of cases which he considered conclusive are likewise open to very considerable doubt.

Now the possibility of ovarian pregnancy is universally admitted, and even so rigorous a critic as Webster has abandoned his skepticism, and has reported two authentic cases.

Williams also said he had carefully gone over the literature upon ovarian pregnancy, and has classified the cases reported up to January, 1906, as positive, highly probable, fairly probable, and doubtful, according to the extent to which Spiegelberg's criteria were fulfilled. He was able to find 13 specimens belonging to the first category, which were thoroughly described, and so carefully studied microscopically that their ovarian origin was conclusively demonstrated; namely, the cases of Gottschalk, 1893; Ludwig, 1896; Kouwer and Tussenbroek, 1899; Croft, 1900; Anning and Littlewood, 1901; Robson, 1902; Franz, 1902; Thompson, 1902; Mendes De Leon and Holleman, 1902; Micholitsch (2 cases), 1903; Boesebeek, 1904; and Webster, 1904. The patients of Gottschalk and Ludwig had gone to term, but in none of the other 11 had the pregnancy progressed beyond the fourth month. Since then many more positive cases have been described. Lockyear reported 2 personal cases in 1917. Meyer and Wynne have since reported an additional case and analyzed the literature up to 1919.

It is interesting to note that in one-third of the positive or highly probable cases which Williams collected, the pregnancy had gone to full term, and in several instances had eventuated in the formation of lithopedia, which had been carried for years before being removed. This would appear to indicate that the ovary can accommodate itself more readily than the tube to the growing pregnancy; but rupture at an early period is the usual termination.

Probably a great number of specimens come to the pathologist at a time when the pregnancy is advanced and the anatomical relations are so distorted by the fetal sac that it is difficult to make the specimen fulfill all of the requirements for establishing the diagnosis. It is, therefore, very hard to determine how commonly ovarian gestation occurs. It is the author's opinion that ovarian hæmatomata are, in a number of instances, ovarian pregnancies.

Lewis' *System of Surgery* states that up to the present time only 45 cases of undoubted ovarian pregnancy have been reported. There is nothing in the history or examination to differentiate between ovarian and tubal pregnancy except that in the ovarian type the pregnancy usually advances further.

In ovarian, as in tubal gestation, very little decidua is found and when rupture occurs it is usually caused by the invasion of the syncytium into the wall of a blood vessel causing hæmorrhage which overdistends the sac wall. Severe or fatal hæmorrhage into the peritoneal cavity may take

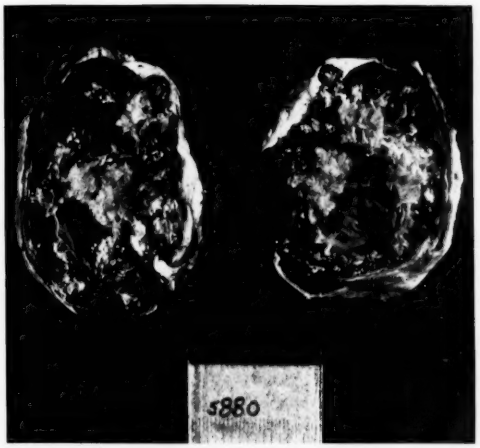


Fig. 1. Photograph of gross specimen laid open showing sac occupying the central area of the ovary.

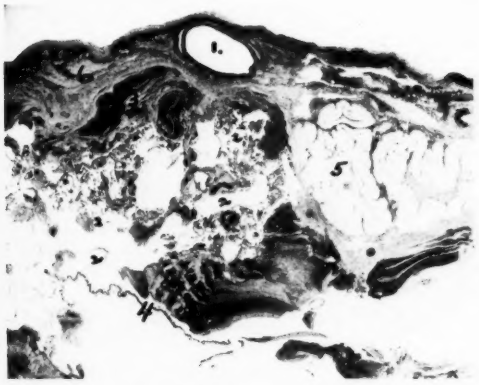


Fig. 2. *1*, Follicle; *2*, villi; *3*, hæmorrhage; *4*, chorionic membrane; *5*, corpus luteum; *6*, ovarian tissue.

place when rupture occurs or bleeding may be slight and the process go on to resolution.

On reviewing the literature on this subject we find that there have been 9 cases reported since 1925. Four of them were reported in British medical journals, 3 in German, and 2 in American medical journals.

Among the recent cases of ovarian pregnancy appearing in British medical journals is one by Franzen and R. S. S. Statham, of the Bristol Royal Infirmary. This was reported in 1927. Their patient was operated on after skipping a second menstrual period and an embryo of 7 millimeters was found in a sac containing a clear fluid. This case appears to be a true ovarian pregnancy, as the historical examination revealed the presence of embryonic tissue surrounded by ovarian tissue and the tube on the affected side was intact.

Another case of ovarian pregnancy was reported by W. W. King in 1926 in the *Journal of Obstetrics* and *Gynæcology of the British Empire*. The microscopic photographs proved the presence of embryonic tissue close to which could be seen corpus luteum. The ovary retained its anatomical relationship with attachments to the uterus and broad ligament. The left fallopian tube which was normal was quite separate and not adherent to the ovary.

Another case was reported in 1926 by Acomb and Canby which was a full time ovarian fetation. This patient was 33 years old, had been married 6 years, and had not heretofore become pregnant. The patient appeared to be about 8½ months pregnant at the time of the first examination. On X-ray examination there appeared to be a fully developed fetal skeleton lying in an extremely irregular position. The head was above the pelvis and the fundus above the crest. The fetal spine formed an acute angle against the abdominal wall of the mother. The skeleton appeared to lie in a more ventral position than normal. On operation the uterus itself was found in the pelvis and was slightly enlarged. The right fallopian tube was stretched over the sac, and the tissue of the right ovary was thinned out, and constituted the outer layer of the sac. The sac lay above the broad ligament. A full time male child weighing about 7½ pounds was delivered through the incision. The skin was slightly macerated. The child appeared to have been dead for 2 or 3 weeks.

In 1928, a report of ovarian pregnancy appeared in British literature and was reported by Banister J. Bright. The patient was admitted as one of a right pyosalpinx. She had skipped one menstruation. Her symptoms corresponded to the usual symptoms of ectopic pregnancy. On examination a mass was felt to the right of the uterus. Microscopically the specimen appeared to be one of ovarian pregnancy. The four criteria stated by Spiegelber appeared to have been fulfilled.

Barna reported a case in 1925 which presented the usual symptoms and signs of ectopic pregnancy. This patient developed abdominal hæmorrhage that necessitated immediate operation and the left ovary was found to be enlarged and bluish in color. Grossly and microscopically the specimen appeared to be one of ovarian pregnancy.

Zimmerman, of Germany, reported a case of ovarian pregnancy in June, 1927, which appeared to be one almost identical to the one reported by Barna. There was a rupture of the ovarian tissue and hæmorrhage which necessitated immediate operation. Microscopic examination showed it to be a case of true ovarian pregnancy.

Hellendall, of Germany, reported a case of ovarian pregnancy in November, 1927. His patient had had a miscarriage a year before. Eight days after cessation of her menstruation she experienced severe pains on the left side and slight bleeding. On examination a mass could be felt at the left of the uterus. Diagnosis of ectopic pregnancy was made and operation showed it to be a true ovarian pregnancy.

Among the recent reports in American literature we find one by R. M. Mayne, in 1926. His patient presented the usual symptoms and signs of ectopic pregnancy but it was unusual in that it progressed to a late stage. His patient last menstruated December 23, 1922, and she was operated upon June 30, 1923, at which time a living male child of approximately 27 weeks was extracted. The child lived 10 hours. Macroscopically the structure showed a sac occupying the position of the right ovary and adhesions to sections of the small intestines, sigmoid, uterus, and pelvic floor. The right tube was normal except for the great increase in length. The utero-ovarian ligament, although adherent to the mass, could be seen. The microscopic section of the sac showed a developed ovarian tissue.

James R. Manley reported a case of ovarian pregnancy in 1926. She too presented the usual signs of ectopic pregnancy. The specimen removed was the left ovary containing a hæmatoma about 1½ inches in diameter. The tube on the infected side was intact. The specimen on microscopic examination showed ovarian tissue and a large area of corpus luteum. The embryo itself was a centimeter in length.

A brief report of our case follows:

Mrs. W. M., aged 32 years. The family history was negative. She had had the usual diseases of childhood but no serious illness or any operations. Menses began when she was 13 years old, had always been regular, and appeared every 28 days, lasting 8 days. She gave no history of dysmenorrhœa. She had been pregnant twice before and had gone on to normal deliveries. Her last child was born 5 years ago. She gave no history of pelvic infections.

*Present illness, physical findings, and operation.* Patient was first seen February 17, 1929, at which time she complained of indefinite pain in the left pelvis. She had started menstruating February 10, in a normal manner except that she experienced some slight cramps on both sides. Examination revealed a temperature of 100 degrees F. and a pulse rate of 84. A mass about the size of a lemon could be felt to the left of the uterus. This mass was not adherent to surrounding structures. The leucocyte count showed 13,000; red cell count 3,800,000; and hæmoglobin 80 per cent. There had been no bleeding. Extra-uterine pregnancy was considered but that diagnosis was discarded as patient had never missed a menstruation and the mass was freely movable. There was no nausea and no breast signs. There was, however, a slight uterine enlargement but the cervix seemed normal. The diagnosis of ovarian cyst seemed the most reasonable and it was thought that it was possibly twisted on its pedicle causing tenderness, slight fever, and an increased leucocyte count. The patient was watched for 2 days during which time the pains in the left pelvis became more severe. She was sent to the hospital and operated upon the following day. The mass in the left pelvis was found to be a bluish gray mass, occupying the position of the ovary and was attached to the uterus by the utero-ovarian ligament. The tube on that side was intact and appeared to be normal. The mass was not adherent to any structure. It was removed and the abdomen closed. The patient made an uneventful recovery.

On opening the specimen a sac was found within containing a clear fluid and a gray membrane resembling placental tissue. A small grayish body suspended on a pedicle was seen. A section of the placental tissue was sectioned and stained and examined under the microscope. Chorionic villi were demonstrated by their layers of syncytial and Langhans' cells. The gross specimen was sent to Dr. George Streeter, director of the embryology department of the Carnegie Institute. His report is as follows:

"I am enclosing photographs of your specimen which prove very conclusively the specimen to be one of ovarian pregnancy. In the photographs one can clearly recognize the corpus luteum, graafian follicles, and typical ovarian tissue embedded in which is the ovum with normal appearing chorion and chorionic villi. The photograph of the gross slide laid open in the midline gives the appearance of the total chorionic sac occupying the central area of the ovary. Around the tips of the villi there is more or less extravasation typical of implantation areas."

All of Spiegelberg's criteria were fulfilled in this case. The tube on the affected side was intact, the sac occupied the position of the ovary, it was connected to the uterus by the utero-ovarian ligament, and ovarian tissue was found completely surrounding the sac.

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# SUBMUCOUS LIPOMATA OF THE GASTRO–INTESTINAL TRACT

## REPORT OF TWENTY–EIGHT CASES[1]

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BENIGN tumors of the gastro-intestinal tract arouse interest because of their comparative rarity. They deserve careful consideration because of the excellent prognosis following excision and the less radical surgical procedure which often can be adopted if they are recognized before operation or at the time of operation.

The observation recently at the clinic of a lipoma of the ascending colon, producing obstructive symptoms, renewed my interest in that subdivision of benign gastro-intestinal tumors. A study was made of this, as well as other cases occurring at the clinic, of those cases described by other authors, and of the pathological material, both that obtained at operation and at necropsy. The importance, as well as the absence of a comprehensive review in English, of this group of tumors since 1909 encouraged me in the idea of presenting in abstract reports of cases that have been published and of those which have occurred at the clinic.

Lipomata of the gastro-intestinal tract are divided anatomically into two groups, the submucous and the subserous. A small number are both submucous and subserous. The submucous variety is more common. The not uncommon development of subserous lipomata from appendices epiploicæ, and the origin of symptoms from the size and weight of the tumor (as well as from the difference in situation) makes it advisable that the two groups be considered separately, from the clinical and pathological, as well as from the anatomical, standpoints. It has seemed expedient to confine the present review to the submucous group.

The submucous lipomata which have been observed at the clinic can be divided into two groups. Group 1 is composed of those tumors which produced symptoms. They are four in number. One of these, a gastric lipoma, has been reported recently by White and Judd, and the case will not be reported here. The 3 remaining tumors were in the large bowel. One of these (Case 1), a lipoma of the sigmoid mentioned briefly by King, is of sufficient interest to warrant a complete account of the case. Group 2 is composed of 25 tumors which did not produce symptoms; one mentioned by King, which was observed incidentally at operation, has been included; the 24 others were found in the course of 3,924 consecutive necropsies.

### REPORT OF CASES IN GROUP 1

CASE 1. A man, aged 54 years, registered at the clinic, September 25, 1914, complaining of bowel trouble. The family history and remote personal history were unimportant. Six years previous to registration, for a period of 2 months, there had been constipation, alternating with diarrhœa, and soreness in the left lower quadrant of the abdomen. When he had been constipated, there had been a palpable mass in the left lower quadrant; the mass had disappeared following the action of a cathartic. The diarrhœal stools had contained blood and mucus. No further trouble had occurred until 3 months before registration, when there had been griping pains in the lower part of the abdomen, a sense of obstruction in the left lower quadrant, and stools composed largely of mucus with some blood. During the last week before admission there had not been any bloody mucus.

The systolic blood pressure was 156 and the diastolic 116, measured in millimeters of mercury. There was a somewhat movable, ridge-like mass, 15 to 20 centimeters long in the left lower quadrant of the abdomen. Examinations of urine, blood, and stool, and proctoscopic examination gave negative results. Roentgenological examination

[1]Submitted for publication March 3, 1930.

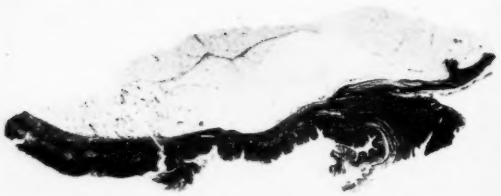

Fig. 1. Lipoma of the sigmoid. Infolding of the muscular layer into the angle between the mucosa and the lipoma is evident. The base is covered by the thinned muscularis, and the free portion by the necrotic mucosa. Case 1.

after a barium enema disclosed an obstruction in the descending colon. A diagnosis of carcinoma of the sigmoid (70 per cent) and diverticulitis (30 per cent) was made.

Abdominal section, September 30, 1914, revealed that intussusception had been present and had been reduced spontaneously before operation. A mass was palpated in the upper part of the sigmoid. Resection of 25 centimeters of the sigmoid and an end-to-end anastomosis were performed.

Examination of the specimen removed at operation revealed a tumor measuring 5 by 4 by 3.5 centimeters, which was attached near the line of reflection of the mesentery by a base measuring 2.5 centimeters in diameter. The mucosa reflected over the tumor was normal in appearance for a distance of 1.5 to 1.7 centimeters. The remaining, lobulated surface of the tumor was covered by a bluish-yellow, smooth layer. Dissection of the thickened subserosa revealed, as seen on cross section, an elevated yellow area surrounded by a groove which separated it from the muscular layers of the wall of the bowel. The tumor was composed of soft yellow tissue, arranged in lobules, separated by narrow bands of more dense and opaque tissue, and discolored immediately underneath the necrotic portion of its surface. The microscopic section (Fig. 1) showed the reflection of the mucosa, muscularis mucosæ, and submucosa over the surface of the tumor. The mucosa was normal, except for the zone of transition which was interposed between the normal mucosa and the necrotic portion. The necrotic portion was composed of fibrin and it held in its meshes dense masses of disintegrating leucocytes. The muscularis

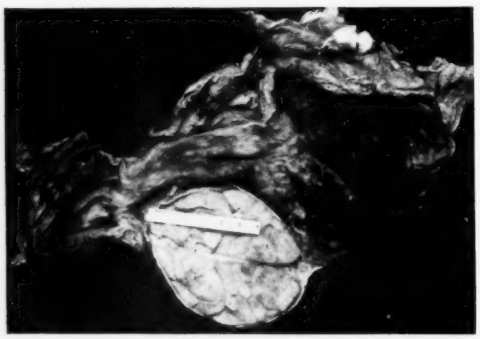

Fig. 3. Large submucous lipoma of the greater curvature of the stomach. Case 5.

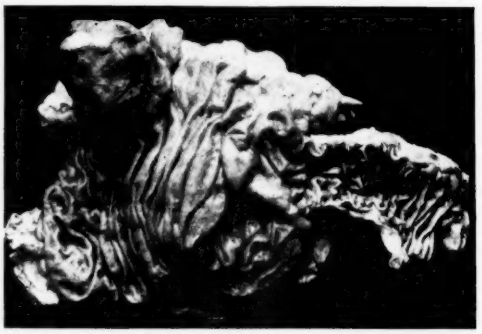

Fig. 2. Submucous lipoma of the ascending colon. Case 3.

muscoæ was traced as a distinct bundle for about half the distance from the wall of the bowel to the level of the zone of transition. The muscular layer was thickened at the level of the bottom of the groove surrounding the base of attachment, and it could be traced in the one direction over the base of attachment of the tumor as a thin layer; in the other direction it was continuous with the muscular layers of the wall of the bowel, forming the outer wall of the groove; along the surface of the tumor the fibers decreased in number to a point a third of the distance between the wall of the bowel and the region of mucosal replacement. At the level of mucosal disintegration, muscle fibers were no longer recognized. In addition to the connective tissue septa, numerous capillaries and a few arteries, with supporting stroma, were present. In the region beneath the necrotic membrane, patches of cells, chiefly erythrocytes, with an occasional leucocyte, were present in the supporting stroma.

Convalescence was uneventful. June 19, 1915, the patient stated by letter that, aside from constipation and a small postoperative ventral hernia, he was in excellent health.

The obstructing nature of the lesion was apparent. The early history of distress in the left lower quadrant, could it have been proved to be a result of the lesion which was causing trouble at the time of examination, would have pointed to a non-malignant process of long duration. Diverticulitis, or a carcinoma, might have caused the more recent symptoms. The age of the patient and loss of weight are compatible with each. The rarity of intussusception, and the lack of distinctive features, justified hardly more than passing consideration of this possibility. The more justifiable assumption was that carcinoma was present.

Case 2. A woman, aged 39 years, entered the clinic June 30, 1926, complaining of severe attacks of pain in the upper part of the abdomen. The family history, remote personal history, and menstrual history were unimportant. One year previous to examination, bloating and epigastric distress after meals made it necessary for her to avoid heavy foods, meat, and cabbage. Two months before she registered at the clinic, during an attack of influenza, the

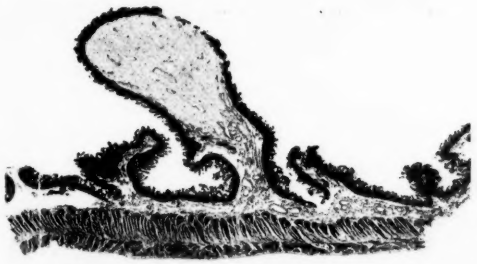

Fig. 4. Cross section of a small lipoma attached by a short fibrous pedicle to a plica circularis of the jejunum. Case 12. (Hæmatoxylin and eosin, ×5.)

first attack of severe pain had occurred. There had been two attacks since, the last, 2 weeks before registration. The pain was in the right part of the epigastrium and spread to the lower part of the abdomen and through to the back. The last attack had lasted 5 days, during which time she had vomited constantly a greenish, bitter fluid, and had been obstinately constipated.

The patient's height was 61.5 inches; her usual weight was 130 pounds, and her weight at the time of examination was 105 pounds. Blood pressure, pulse rate, and temperature were normal. There was a large, firm mass in the right side of the abdomen, in the region of the ascending colon. The mass was movable. Examination of the urine and blood, and the Wassermann reaction of the blood gave negative results. Roentgenological examination after a barium enema revealed a large filling defect at the hepatic flexure, and marked obstruction. A diagnosis of carcinoma of the colon at the hepatic flexure was made.

The specimen obtained at operation was a cup-shaped section of large bowel; one side of the cup was cut away to display the tumor. The thickened, œdematous condition of the wall of the bowel incident to circulatory changes wrought by the operative procedure was striking. The tumor was cauliflower-shaped. It measured 7.5 by 3.5 centimeters and extended 4.5 centimeters into the lumen of the bowel. Its base of attachment measured 4.5 by 2 centimeters. It was composed of yellow tissue arranged in irregular lobulations and was covered completely by normal mucosa. In microscopic section were seen normal mucosa, submucosa, and muscularis mucosæ reflected from the wall of the bowel over the tumor, and infolding of the muscular layer for a short distance in the area between the reflected mucosa and the surface of the tumor. The microscopic structure of this tumor was similar to that in Case 1. In addition, œdema, cellular infiltration, and great thickening of the wall of the bowel, especially of the subserous layer, were present.

September 28, the opening made at colostomy was finally closed after curettage. In January, 1927, the patient's general condition was excellent. A small, pinpoint opening remained at the site of colostomy.

None of the features of the case pointed to the benign nature of the obstructive lesion. The preponderance in incidence of carcinoma of the colon over all other tumors of the colon as a cause of obstruction made reasonable the assumption that a carcinoma was obstructing the bowel.

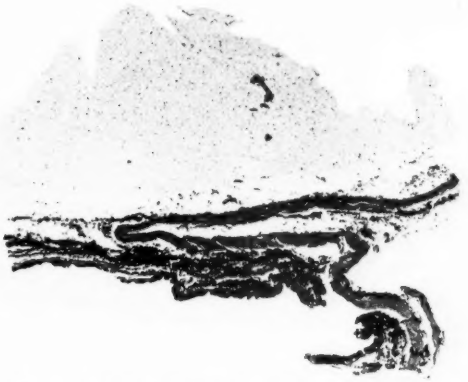

Fig. 5. Section through the periphery of the lipoma. The intra-intestinal pressure has caused the serosal surfaces overlying the tumor and the surrounding wall of the bowel to touch, and has produced an arrangement of the muscle layers suggesting infolding, an earlier stage of that seen in Figure 1. Case 20. (van Gieson's stain, ×8.)

Case 3. A woman, aged 43 years, was referred to the clinic, November 30, 1928, because of epigastric pain and a round firm mass 10 centimeters in diameter and slightly movable in the left upper part of the abdomen. The family, marital, and menstrual histories were negative. There had been distress high in the epigastrium for a number of years, at irregularly occurring periods. During the last month before registration at the clinic, severe epigastric pain, more severe between meals, had been present at times; the patient had vomited every 2 or 3 days; constipation had appeared at the onset. Diarrhœa had occurred for one day. Blood had not been present in the stools.

There was a large, rounded, apparently smooth, moderately movable, and slightly tender mass in the left side of the abdomen at the level of the umbilicus. Examination of the urine, and the Wassermann reaction of the

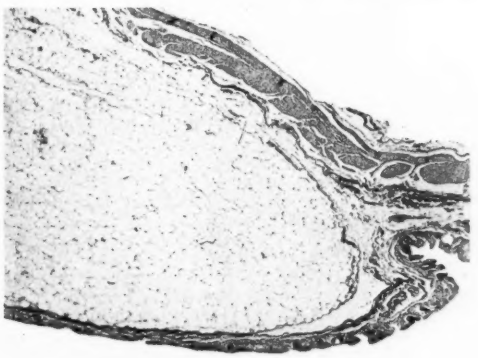

Fig. 6. A cross section, showing the typical lipomatous structure of the tumor, its submucous situation, and the displacement of the muscularis peripherally, as well as of the mucosa centrally. Case 23. (van Gieson's stain, ×12.)

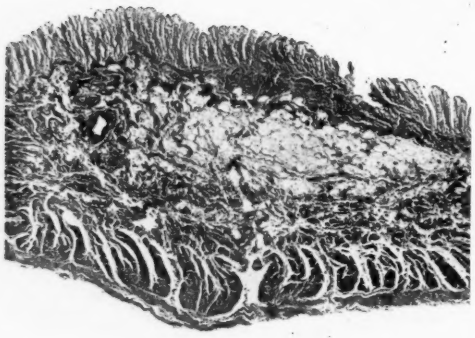

Fig. 7. A small collection of fat cells in the submucosa. Case 26. (Hæmatoxylin and eosin, ×12.)

Fig. 8. Diffuse lipomatous infiltration of the submucosa of the superior labium of the ileocæcal valve. Case 27. (van Gieson's stain, ×5.)

blood gave negative results. The concentration of hæmoglobin was 40 per cent; erythrocytes numbered 4,790,000 and leucocytes 9,700 in each cubic millimeter of blood. The differential count was negative. Roentgenological examination of the thorax gave evidence of healed lesions of tuberculosis of the upper lobe of the left lung; roentgenograms of the kidneys, ureters, bladder, and stomach gave negative results. Roentgenological examination of the colon showed a polypoid defect at the hepatic flexure. After castor oil had been taken, the mass in the left side of the abdomen had disappeared; then a mass had been palpated in the region of the ascending colon. This mass became palpable only with difficulty after further purging. A diagnosis of partial intestinal obstruction due to a polypoid lesion of the ascending colon was made.

December 17, 1928, exploration through a right rectus incision revealed a polyp about 6 centimeters in diameter in the ascending colon. Resection in two stages was decided on. Ileocolostomy was performed and, January 5, 1929, this was followed by resection of the cæcum and ascending colon.

The specimen obtained at operation (Fig. 2) was an irregularly lobulated polypoid tumor, 4.5 by 4 by 3 centimeters. The mass was attached to the mesial wall of the ascending colon, approximately 10 centimeters above the ileocæcal valve, by a base which measured 2 by 1 centimeters. The mucosal covering of the tumor had a normal appearance, except for the free end, where there was an area which extended more onto the superior and anterior surfaces. In this area the mucosa was absent and the color yellow. There was a linear, healed scar, 0.5 centimeter in length, on the inferior surface. On the serosal surface, opposite the point of attachment of the tumor, there was a deep dimple filled with areolar connective tissue and large blood vessels. On section, the tumor was found to be composed of yellow adipose tissue separated into lobules by bands of more dense opaque tissue; the area of attachment of the tumor to the muscular layer had a diameter of 0.5 centimeter, and the bulging into the dimple was surrounded by a groove. The angle between the mucosa and the surface of the tumor was filled with areolar tissue. The normal mucosa was separated from the yellow area on the free end of the tumor by a narrow, necrotic zone. The muscularis mucosæ could be traced almost to the zone of mucosal necrosis. The arrangement of the muscular layer was similar to that seen in Cases 1 and 2. The capsule, which was indistinguishable from the submucosa, and the septa, contained numerous collections of leucocytes, mostly polymorphonuclear leucocytes, but also small and large mononuclear leucocytes which in places invaded the adipose structure.

Convalescence was uneventful. The patient was dismissed, January 28, 1929.

The presence of the polypoid type of lesion was established by roentgenological examination. The changing site of the tumor suggested that it had a long pedicle or that intussusception was present. The long pedicle did not exist. In spite of the fact that no evidence that intussusception previously had existed was found at operation, intussusception seems to offer the only possible explanation of the events. The possibility that the polyp was benign was considered because of the existence, for years, of epigastric pain. The fact that adenomatous polyps are observed more frequently than are all other types made it probable that such a polyp was being dealt with here. An adenomatous polyp as large as the one found in this case usually is carcinomatous and demands wide removal of lymph nodes.

### REPORT OF CASES IN GROUP 2

In this group of cases, the tumors did not produce symptoms. All of the reports, except in Case 14, are made on the basis of changes found at necropsy.

Case 4. A male subject, aged 64 years. A sessile mass 1 to 1.5 centimeters in diameter, was found. It was composed of adult fat cells, and was situated at the lesser curvature of the stomach, 6 centimeters from the pylorus, in the submucosa, and was covered by normal mucosa and muscularis mucosæ.

Case 5. A male subject, aged 67 years. A sessile mass, 9.5 by 4.5 centimeters, was situated at the greater curvature of the stomach. The mass extended onto the anterior and posterior walls of the stomach (Fig. 3), and distally to within 1 or 2 centimeters of the pylorus, projecting 5.5 centimeters into the lumen. It was composed of adult fat cells, was separated into lobules by connective tissue

septa, was enclosed in a fibrous capsule continuous with the submucosa, and separated hypertrophied muscular layers externally from the hypertrophied muscularis mucosæ and normal mucosa internally. Occasional groups of four to eight small mononuclear cells were present in the supporting structures of the capillaries and occasionally in that of an arteriole.

CASE 6. A female subject, aged 65 years. A submucous lipoma, 8 millimeters in diameter, was found on the lesser curvature of the stomach.

CASE 7. A male subject, aged 74 years. A soft, yellow, submucous, sessile, pyriform gastric lipoma, the apex of which extended onto the pyloric ring, was found. It was attached by a base 3.5 centimeters long and 2 centimeters wide, which were the greatest diameters of the tumor. It was raised 1 centimeter above the mucosal surface and was covered by thinned but otherwise normal mucosa.

CASE 8. A female subject, aged 63 years. A soft, yellow, fatty, duodenal polyp, measuring 3 by 1 by 0.4 centimeters, flattened in the proximal and distal directions, was discovered. It was attached by a narrow pedicle composed of fibrous tissue and normal mucosa to a prominent plica circularis at a point 1 centimeter lateral to the ampulla of Vater. It was covered with thinned but otherwise normal mucosa.

CASE 9. A male subject, aged 81 years. A small, submucosal, finely granular, yellowish-white duodenal lipoma was attached to the free edge of a plica circularis.

CASE 10. A female subject, aged 64 years. Two soft, yellow, duodenal lipomata, covered with normal mucosa, were found. They were situated 1 centimeter and 3 centimeters, respectively, below the ampulla of Vater on the posterior wall. The upper polyp measured 2 by 1.5 by 0.4 centimeter, and was attached by a flattened pedicle, 1.5 centimeters broad, to the free edge of a plica circularis. The lower polyp measured 0.5 centimeter in diameter, and was similarly attached.

CASE 11. A male subject, aged 78 years. There was a duodenal lipoma, measuring 1.4 by 1.3 by 0.8 centimeter, attached by a short pedicle to a plica circularis just below the ampulla of Vater.

CASE 12. A male subject, aged 61 years. A lipoma, 8 by 3 by 4 millimeters, was found (Fig. 4). It was situated in the first part of the jejunum, and was attached by a short fibrous pedicle to a plica circularis. Occasional groups of several fat cells were present in the submucosal layers of the neighboring plicæ circulares.

CASE 13. A female subject, aged 61 years. There was a lipoma of the jejunum, 1 centimeter in diameter.

CASE 14. A woman, aged 37 years, underwent resection of the cæcum, ascending colon, part of the transverse colon, and 6 centimeters of ileum for colitis. A submucous lipoma was found 5 centimeters proximal to the ileocæcal valve.

CASE 15. A male subject, aged 21 years. Six submucous lipomata were scattered irregularly over 40 centimeters of the lower part of the ileum, of which the largest measured 1 by 1.5 centimeters. They were sessile, whether or not they were within a plica circularis. Associated findings were multiple subcutaneous lipomata, multiple lipomata of the dura, and abnormalities of the hands and nails.

CASE 16. A male subject, aged 53 years. There was a submucous, sessile lipoma of the ileum, 8 by 8 by 6 millimeters.

CASE 17. A male subject, aged 43 years. A soft, yellow lipoma, measuring 8 by 10 by 12 millimeters, was found. It was attached by a short pedicle in the lower part of the ileum, which was continuous with a poorly developed plica circularis. There was slight dimpling of the serosa opposite the point of attachment of the pedicle. The mucosa was normal.

CASE 18. A female subject, aged 48 years. A small, sessile lipoma of the cæcum, measuring 7 by 7 by 6 millimeters, was found.

CASE 19. A female subject, aged 63 years. A submucous lipoma of the cæcum, measuring 10 by 10 by 4 millimeters, was found.

CASE 20. A male subject, aged 63 years. A submucous lipoma was situated on the lateral cæcal wall, 2 centimeters above the level of the ileocæcal valve. It measured 4.5 by 1.5 by 2 centimeters. Its long axis was transverse to the axis of the bowel, and it was attached by a base which measured 4 centimeters in one diameter and 1 centimeter in another diameter. The place of attachment was seen on the serosal surface as a yellowish area. The muscular coat, as previously described, was folded internally, separating the mucosa and the surface of the tumor for a short distance (Fig. 5).

CASE 21. A male subject, aged 35 years. A lipoma of the cæcum, 1 centimeter in diameter, was present.

CASE 22. A male subject, aged 65 years. A yellow, lipomatous polyp, which measured 1.5 by 1 by 1 centimeter, was found. It was attached by a pedicle 1 centimeter in length to a plica semilunaris coli, 10 centimeters distal to the ileocæcal valve.

CASE 23. A male subject, aged 65 years. A flattened, sessile lipoma, measuring 15 by 12 by 4 millimeters, was found in the ascending colon (Fig. 6). Small collections of fat cells on the submucosa gave a yellowish tint to the mucosa about the lipoma and distal to it for a distance of 5 to 6 centimeters.

CASE 24. A female subject, aged 62 years. The mucosal surface of the ascending colon was discolored by a faint, yellow mottling. This was especially pronounced in the area surrounding a sessile lipoma, 1.5 by 1.5 by 0.5 centimeter, that was situated just distal to the ileocæcal valve, on the medial wall of the ascending colon. The superior labium of the ileocæcal valve was yellow, was 1.2 centimeters thick, and extended 1.5 centimeters into the lumen of the bowel. Microscopically, beneath the area of yellow tinted mucosa there was rich infiltration of the submucosa with fat cells. The thickening of the superior labium was due to adipose tissue situated almost entirely on the colic side of the infolding circular muscular fibers.

CASE 25. A female subject, aged 65 years. A sessile, submucous lipoma, measuring 1 by 1 by 0.4 centimeter, was situated 4 centimeters distal to the ileocæcal valve. Submucosal infiltration gave a yellowish tint to the mucosa, as in Case 16. Thickening of the margin of the ileocæcal valve gave the appearance of a ring with a small os, due to fat deposited both on the ileal and on the colic sides of the infolded circular fibers.

CASE 26. A female subject, aged 70 years. There was thickening of both margins of the ileocæcal valve, so that the valve appeared as a slit. The mucosa was tinted because of deposits of fat, as in Case 25, but more marked. There were three sessile lipomata, one in the cæcum, 1.5 by 2 by 0.4 centimeter, and two in the ascending colon, 1.5 by 1.3 by 3 centimeters, and 2.5 by 2 by 0.5 centimeter. Five other small lipomata, as well as numerous areas in which there was a more marked yellowish tint, with underlying small collections of fat, were found (Fig. 7).

CASE 27. A male subject, aged 51 years. Fatty thickening of the superior labium of the ileocæcal valve (Fig. 8) and a submucous lipoma of the upper part of the sigmoid, 2 centimeters in diameter, were found.

CASE 28. A male subject, aged 81 years. A lipoma in the submucosa of the rectum, 1 centimeter in diameter, was present.

PREVIOUSLY PUBLISHED REPORTS

Stetten, in 1909, made a comprehensive review of the previously reported cases and presented 2 of his own. He tabulated the main points of interest in 77 cases in such a satisfactory way that it appears superfluous to do more than refer the interested reader to his paper for the abstracts of these cases. However, it could not be determined with certainty that the single cases each of Marchand, Zum Busch, and Ray, which Stetten included, were not of the subserous variety, and these are excluded from the total series of submucous lipomata. White and Judd, in 1929, found reports of 13 cases of submucous gastric lipoma and reported 1 case which had occurred recently at The Mayo Clinic. Three of 13 cases, reports noted in the literature by White and Judd, have been included by Stetten in his series. To their paper the interested reader is again referred for a résumé of those cases. Careful search has revealed reports of eight cases of gastro-intestinal lipoma published prior to the date of Stetten's paper and not included by him, and reports of 4 cases of gastric lipoma not included by White and Judd. In addition, 56 cases of intestinal lipoma have been reported since 1909. A total series of 153 reports of cases of gastro-intestinal submucous lipoma previously published is made available for study by reference to the papers of the authors mentioned and to the following abstracts.

In the previous paragraphs, it has been noted that of the 77 cases reported by Stetten, 3 have been omitted from this review. Certain other cases included in other authors' series have not been included. The cases of Levadina, of Power, and of Thorek have been excluded, because the tumors were not submucous lipomata. Those of Treves, of Brohl, and of Kaseymeyer have been omitted because these authors merely quoted reports of cases given by other writers. Moreover, the specimens in the Birmingham Museum, in the Museum of the Royal College of Surgeons, and in the Leeds Museum, mentioned by Bland-Sutton, and in the London Hospital Museum, mentioned by Treves, have not been included since it was not possible to ascertain that those specimens did not belong to cases already included.

CASE 29. Cruveilhier's case, 1835–1842. The tumor was a sessile lipoma, about 2.5 by 2 by 1 centimeters, covered by intact mucous membrane. It was situated near the pylorus.

CASE 30. Brunner's case, 1897. The patient was a man, aged 51 years. He experienced severe pain for 5 days and did not pass fæces or flatus. There was abdominal distention and a bloody mucoid discharge. On rectal examination, a pedunculated tumor was found above the anus, attached inside of the bowel, that was invaginated into the rectum. At operation, the tumor and part of the invaginated bowel were removed, and the opening was closed by suture. Colostomy was performed on the following day. Later, the opening made at colostomy was closed. The diagnosis was submucous lipoma. Cure was effected.

CASE 31. Garre's case, 1898 (briefly described by Mattes, 1909). The patient was a women, aged 75 years. Abdominal pain had lasted 8 days before diarrhœa without blood appeared, and continued for 3 weeks. Anorexia and emaciation followed. A kidney-shaped tumor was found near the umbilicus, at the left end of which a small, half-ball-shaped tumor could be distinguished. Laparotomy disclosed chronic ileocolic intussusception, and a tumor at the left end of the intussusception. The intussusception was reduced and 12 centimeters of the intussusceptum was resected. A submucous lipoma about 2.5 centimeters in diameter was found 2 centimeters from the ileocæcal valve. Cure was effected.

CASE 32. Haasler's case, 1902. The patient was a man, aged 25 years. He had had belching and heart-burn for years. Three months before operation, severe umbilical pain and diarrhœa had occurred for 1 day. Since then colicky pain had been increased in severity by food. Rigidity and tenderness in the umbilical region were noted. The patient had vomited 2 days before admission. A tumor near the umbilicus, which was tender on palpation, moved to and fro with respiration. Pain and diarrhœa, with blood and mucus in the stool, persisted. At laparotomy, intussusception of the transverse colon and numerous adhesions were found. Resection was performed with anastomosis, by the Murphy button. At the apex of the intussusception was a submucous lipoma, attached by a broad pedicle and covered by gangrenous mucosa. The patient recovered.

CASE 33. Lorenz' case, 1906. The patient was a man, aged 58 years. Abdominal pain, symptoms of obstruction, and loss of weight were complained of. A sausage-shaped mass extending across the upper part of the abdomen, which hardened under palpation, and a tender tumor, 5 centimeters in diameter, at the left end of this mass, were palpated. Laparotomy disclosed invagination of the ileum, cæcum, and ascending colon. The intussusception was reduced. A pedunculated submucous lipoma about 5 centimeters in diameter, covered by ulcerated mucous membrane and attached to the lateral cæcal wall opposite the ileocæcal valve, was removed. Cure followed.

CASE 34. D'Este's case, 1906. The patient was a man, aged 54 years. Two months previously intense pain had occurred in the right lower quadrant of the abdomen, lasting 3 hours. The pain had recurred at irregular intervals for 2 weeks; it was of short duration and was followed by alternating constipation and diarrhœa. A tumor was palpated in the right side of the abdomen; it moved with respiration. It appeared smooth and ovoid, its long axis running from above and to the right downward to the left. The size of the tumor between attacks was about 3 by 5 centimeters; it was larger during attacks, and tender. Active peristaltic movements progressed from the tumor to the left. The colon was incised at the hepatic flexure. A pear-shaped submucous lipoma, inserted by a broad base and covered by ulcerated mucosa, and the involved segment were removed. The patient recovered.

CASE 35. Mattes' case, 1909. The patient was a man, aged 76 years. Constipation alternating with bloody diarrhœa, and pain in the lower part of the abdomen had been present for 3 weeks. For 4 days a pedunculated tumor about 4 by 6 centimeters appeared through the

anus repeatedly after replacement. Gas did not pass by rectum. The abdomen was distended. At laparotomy, intussusception of the sigmoid into the rectum, and a palpable tumor in the sigmoid were found. The intussusception was reduced. A pedunculated, partly necrotic, submucous lipoma, covered by necrotic membrane, and 14 centimeters of bowel were resected. The patient died.

CASE 36. Francini's case, 1909. The patient was a man, aged 55 years. A diagnosis was made of carcinoma of the stomach with lymphatic involvement. Gastro-enterostomy and resection of two small submucous lipomata of the jejunum was carried out. The jejunal wall was hypertrophied. A similar nodule was not resected. The end-results were not given.

CASE 37. Westbrook's case, 1910. The patient was a woman, aged 34 years. For 1 year she had had attacks of epigastric cramping pain, combined with symptoms supposed to originate in the stomach. The pain was lessened by gastric lavage. One month previous to operation, severe abdominal cramping, radiating from the right to the median line, loose bowels in place of constipation, bloating, and flatulence had gradually developed. A mass, about 6 by 5 by 5 centimeters, was found to the right and on a level with the umbilicus. The mass shifted to the left of the median line when the patient was lying on the left side. Laparotomy disclosed a dilated, thickened, and inflamed ascending colon which enclosed an egg-shaped tumor 5 centimeters above the cæcum. The mucosa of the colon was ulcerated. Resection of the cæcum and ascending colon was carried out. Side-to-side anastomosis was performed, and a lipoma attached to the mesenteric border by a pedicle half the length of the tumor was removed. Recovery was effected.

CASE 38. Finney's case (reported by Wharton, 1911). The patient was a man, aged 35 years. Five weeks before operation, he had had a sudden attack of abdominal pain, followed by a blood-streaked stool. Frequent attacks of left sided pain occurred during the remainder of the day. An indefinite mass was palpable. The patient had had similar attacks 4 and 3 weeks before operation. For 3 weeks he had had pain in the back and rectum. Pain was elicited on pressure and muscular rigidity was found in the left part of the abdomen. Laparotomy disclosed a mass about 6 by 5 by 5 centimeters, just below the splenic flexure. A portion of the wall above the tumor was invaginated. The mucosa was gangrenous and ulcerated. A lipoma about 4 by 3 by 3 centimeters, which was somewhat pedunculated and attached to the mesenteric border, was resected. Recovery was effected.

CASE 39. Ehrlich's case, 1910. A woman, aged 62 years, complained of constipation for a period of 6 months. Eight days before operation, severe pain of the lower portion of the abdomen developed. This was preceded by diarrhœa and a sense of incomplete evacuation, of several days' duration. The pain was more intense on the right side. The patient had been vomiting. Small liquid stools persisted; one stool contained blood. Gas was passed. Muscular rigidity and tenderness were more marked on the right side of the abdomen. There was a firm, tender mass, about 6 centimeters in diameter, in the right lower quadrant of the abdomen. Laparotomy disclosed a firm, sausage-shaped submucous lipoma, about 5 by 2 centimeters, attached by a broad base 15 centimeters orad to the ileocæcal valve. The serosa was dimpled opposite the attachment of the tumor. Ileocolostomy, with resection of 30 centimeters of the ileum, was performed. The patient recovered.

CASE 40. Petit and Malapert's case, 1912. The patient was a woman, aged 32 years. Duration of the symptoms was not given. A blood-stained mucoid discharge persisted; the patient complained of obstinate constipation with frequent desire to defæcate, and tenesmus. There was protrusion of a tumor from the anus. Examination disclosed a bright red, firm, movable tumor, about 4 by 3 by 3 centimeters, situated a few centimeters above the anus, which was attached above to the mucosa of the intussuscepted bowel by a thick long pedicle. The lipoma was covered by ulcerated mucous membrane. The pedicle of the tumor was ligated and cauterized. Reduction of the intussusception was accomplished.

CASE 41. Fantino's case, 1912. The patient was a man, aged 37 years. Three days before operation, severe abdominal pain followed by symptoms of occlusion developed. The abdomen was tympanitic. A few feeble intestinal contractions were noted. There was an enormously distended loop in the lower part of the abdomen. Torsion of the sigmoid, with displacement across the abdomen, was diagnosed. At laparotomy, dilation of the upper part of the colon and intussusception of the transverse into the descending colon were found. Reduction of the intussusception was performed. The colon was incised and a pedunculated submucous lipoma which was attached to the wall of the transverse colon was removed. Colostomy was performed. The patient died.

CASE 42. Rinaldo's case, 1912. The patient was a man, aged 45 years. Twelve hours before examination, he experienced a sudden attack of abdominal pain, followed by a violent movement of the bowel, vomiting, and hiccough. The abdomen was distended, rigid, and tender. A cylindrical, firm, elastic tumor, 8 to 10 centimeters in diameter, extended vertically across the abdomen. Operation disclosed serosanguinous fluid in the abdomen. There was intussusception of 80 centimeters of the small bowel; 215 centimeters of the bowel was resected, and a subserous and submucous lipoma, about 4 by 3 by 3 centimeters at the apex of the area of intussuscepted bowel, was removed. Cure was effected.

CASE 43. Hengstenberg's case, 1913. A woman, aged 21 years, complained of abdominal pain, with tenderness over the cæcum. Appendectomy was performed for a perforating appendix. At operation, appendices epiploicæ up to about 10 centimeters in diameter, and numerous submucous lipomata from 2 to 4 centimeters in diameter, some of which were continuous with the subserous tumors and fatty tumors in the perirectal tissues, were found. Thirty-seven centimeters of the descending colon and sigmoid were resected. The patient died.

CASE 44. Giorgi's case, 1912. A woman, aged 18 years, complained of recurring attacks of severe pain of the right lower quadrant of the abdomen, radiating over the abdomen, of a year's duration. The pain was accompanied by nausea, vomiting, and diarrhœa. Enterorrhagia occurred during the first attack only. A palpable tumor was situated to the right of the umbilicus. It was cylindrical, about 8 centimeters in diameter, and had a lobulated surface. The tumor was movable on respiration and by palpation. Diagnosis of chronic ileocæcal intussusception was made. Laparotomy disclosed intussusception; reduction was impossible. Ileocolostomy was performed, with resection of a short section of the ascending colon, cæcum, and intussuscepted portion of the ileum. A submucous, lobulated lipoma, about 5 by 3 by 3 centimeters, implanted into the ileal wall by a broad base and covered by normal mucosa, was removed. The termination in this case was not stated.

CASE 45. Goodall's case, 1912. The patient was a man, aged 49 years. He complained of recurring attacks, of 1½ years' duration, of intermittent cramping of the upper part of the abdomen. The cramping radiated to the left hypochondrium, and was relieved after 3 or 4

hours by movement of the bowel, or by kneading of a tumor which appeared in either the right or left side of the upper part of the abdomen. This caused disappearance of the tumor and a rumbling, gurgling sound. At laparotomy, intussusception of 15 centimeters of ileum was found. Resection of a pedunculated lipoma, nearly filling the cavity of intussusception, was performed. Recovery was effected.

CASE 46. Randisi's case, 1912. The patient was a man, aged 65 years. Daily, for 28 months, he had vomited 15 minutes after eating. He complained of vague epigastric pain, emaciation, and, lately, mental confusion. Resection of a portion of the stomach, including a triangular, prismatic, yellow submucous lipoma, 2 centimeters above and partially obstructing the pylorus, was performed. Cure was effected.

CASE 47. Collins' case, 1913. The patient was a woman, aged 50 years. For 2 or 3 days, 2 weeks previous to examination, she had had attacks of pain in the right lower quadrant of the abdomen several times daily, accompanied by nausea and vomiting. Following this attack, there had been a blood-stained mucoid discharge four or five times a day. Examination revealed a fixed, oblong mass lying obliquely in the left lower part of the abdomen. Laparotomy disclosed intussusception. Reduction of the intussusception was accomplished. A solid, round, pedunculated lipoma, 5 centimeters in diameter, attached to the inner wall of the cæcum, was removed. Recovery was effected.

CASE 48. Andrée's case, 1913; (also Hohmeier's case, 1913). The patient was a woman, aged 66 years. She had had recurring attacks of cramping of the lower part of the abdomen, vomiting, and constipation, of 5 weeks' duration. The abdominal wall was tense and painful on pressure. Peristalsis and a tumor in the right portion of the abdomen were present. Laparotomy disclosed intussusception of 20 centimeters of ileum into the colon. Resection was performed, with side-to-side anastomosis. A submucous lipoma, about 1.5 centimeters in diameter, attached to the apex of the region of intussusception, was removed. There was some inflammatory reaction in the tumor. Recovery was effected.

CASE 49. Cicala's case, 1913. The patient was a woman, aged 59 years. She had had an intense burning sensation in the hypochondrium after meals; later, paroxysmal pain and a swelling near the umbilicus, which increased in size after ingestion of food, had developed. A soft, elastic, cylindrical, movable tumor, tender only on firm palpation, was found. Laparotomy disclosed intussusception of the cæcum into the transverse colon. The intussusception was reduced. A soft, elastic, yellow, submucous lipoma of the cæcum, about 8 centimeters in diameter, was removed by two lozenge-shaped incisions. Recovery was effected.

CASE 50. Tromp's case, 1915. The patient was a woman, aged 32 years. She had had recurring attacks of gall-stone colic for 4 years; during this time she had had five attacks of generalized abdominal pain with symptoms of obstruction. Examination revealed an oblong, smooth, tender mass, about 10 centimeters in diameter, attached to an enlarged liver, and a smaller tumor in the right lower quadrant of the abdomen, which had disappeared by the following day. Laparotomy disclosed hydrops of the gall bladder. Cholecystectomy was performed. Twenty days after operation, there was recurrence of the obstructive symptoms and a tumor in the right lower quadrant of the abdomen. Laparotomy revealed intussusception of the ileum into the cæcum; the apex was in the transverse colon. Reduction was effected until the apex was in the ascending colon. Resection and ileocolostomy were performed. A submucous lipoma covered by ulcerated mucous membrane 4 centimeters in diameter, situated 20 centimeters above the ileocæcal valve, and attached by a pedicle 8 centimeters long and 3 centimeters thick, was removed. Recovery was effected.

CASE 51. Harrigan's case, 1916. The patient was a man, aged 50 years. For 2 weeks he had had sharp, cramp-like pains in the epigastrium, radiating to the right lower quadrant of the abdomen, occurring two or three times a day at the onset, and increasing until they occurred every 30 minutes and were accompanied by vomiting when the patient was admitted to the hospital. Examination disclosed distention and a tender mass in the right lower quadrant of the abdomen. Leucocytes numbered 14,600 in each cubic millimeter of blood, 85 per cent of which were polymorphonuclear leucocytes. The temperature was 100 degrees F. At laparotomy, ileocæcal intussusception was reduced. The bowel was incised 75 centimeters from the ileocæcal valve, and a soft submucous pedunculated lipoma, 6.5 by 6.5 centimeters, which was attached at the mesenteric border, was removed. Recovery was effected.

CASE 52. Kellert's case, 1917. The patient was a man, aged 46 years. He gave a 6 months' history of abdominal cramping, which was most marked in the epigastric region, constipation, and loss of weight of 20 pounds. A tumor was palpable in the right side of the abdomen. At laparotomy, the cæcum, ascending colon, and a portion of the ileum were resected. Ileocolostomy was performed. A spheroidal, sessile lipoma of the cæcum, 3 centimeters in diameter and covered by necrotic mucosa, was removed.

CASE 53. Lewisohn's case, 1918. The patient was a woman, aged 50 years. For 2 months she had had short attacks of severe, intermittent, right abdominal pain with abdominal distention between attacks. There was no blood in the stools. A round, movable, nodular mass at the level and to the right of the umbilicus was palpated. Roentgen-ray examination disclosed a tumor protruding into the ascending colon. At laparotomy, resection, and lateral anastomosis were performed. A pendulous lipoma, about 3 centimeters in diameter, on the inner wall of the ascending colon, was removed. The base of the tumor was soft; the distal portion was hard, nodular, and gangrenous. Recovery was effected.

CASE 54. Nigst's case, 1918. The patient was a man, aged 55 years. About 1 month before operation, there was onset of pain, which at first was mild, inconstant, and situated at the left of the umbilicus and accompanied by constipation; later the pain increased, the stools became small, and diarrhœa developed. A tumor, about 6 centimeters in diameter, somewhat spindle-shaped, movable, smooth, and of firm, elastic consistence, was palpated. At laparotomy, a portion of the descending colon just below the splenic flexure was resected, and an end-to-end anastomosis was performed. A submucous lipoma covered by normal mucous membrane and attached by a short, thin pedicle to the lateral wall of the bowel was removed. There was dimpling of the serosa opposite the point of attachment of the pedicle. Recovery was effected.

CASE 55. Landauer's case, 1919. The patient was a man, aged 59 years. Seventeen months previous to examination, he had had anorexia, constipation, vomiting, and a sensation of pressure, for 2 months. These symptoms had recurred 9 months later. He had been unable to work thereafter. An indefinite tumor, about 3 centimeters in diameter, above the umbilicus, was palpated. Laparotomy disclosed intussusception, with a mushroom-shaped lipoma, 5 by 3 centimeters, attached by a broad pedicle in the ascending colon and enucleated extramucosally. Recovery was effected.

CASE 56. Brouwer's case, 1921. The patient was a man, aged 45 years. He gave a history of chronic intermittent ileus for a period of 4 years. Examination disclosed a cylindrical tumor in the ileocæcal region, the site, size, and consistence of which varied considerably. At laparotomy, the ileocæcal valve and 10 centimeters of ileum was resected. A pedunculated lipoma, about 2 centimeters in diameter, attached to the ileocæcal valve, was removed. Results were not given.

CASE 57. Schneller's case, 1920. The subject was a man, aged 55 years, whose death was the result of pulmonary tuberculosis. Ninety submucous lipomata, varying from a very small size to 1.5 centimeters in diameter, some of which were pedunculated and some sessile, and covered by normal mucous membrane, were distributed through 120 centimeters of bowel, starting at a point 20 centimeters below the duodenum.

CASE 58. Compton's case, 1920. The patient was a woman, aged 30 years. Constipation had persisted for many years. Examination revealed a lipoma in the fold of the ileocæcal valve; passage from the ileum to the cæcum was through a ring of fat covered by attenuated mucous membrane. Excision of the cæcum was performed. Cure was effected.

CASE 59. Greenwood's case (reported by Bland-Sutton, 1920). The patient was a woman, aged 31 years. Operation revealed a lipoma, 4 centimeters in diameter, covered with ulcerated mucous membrane and attached by a short pedicle in the ascending colon. The cæcum and adjacent colon were resected.

CASE 60. Balgarnie's case, 1920. The patient was a woman, aged 68 years. She had had life-long constipation. For 2 years she had had abdominal pain and increased constipation and had lost 23 pounds in weight. She complained of pain and vomiting. At laparotomy, intussusception of the small bowel was reduced. The wall of the bowel was incised over a pedunculated lipoma, about 5 centimeters in diameter, and the tumor was removed. The involved portion of the bowel was resected and an end-to-end anastomosis was performed. Cure was effected.

CASE 61. Labey's case, 1920. The patient was a woman, aged 46 years. She had had three attacks of abdominal pain, with mucoid evacuations, in the last 4 years. At the time of examination, an attack was of 12 days' duration. Colicky pain with obstinate constipation and melæna persisted. Roentgenograms disclosed obstruction in the middle part of the transverse colon. At laparotomy, a movable tumor, about 6 centimeters in diameter, in the superior part of the ascending colon, was found; the transverse colon was distended. Cæcostomy was performed. Twenty-seven days after operation, incision of the intestine was done. A submucous lipoma, about 4 by 3 by 3 centimeters, attached by a broad base and covered by ulcerated mucous membrane was excised. Recovery was effected.

CASE 62. Longo's case, 1920. The patient was a woman, aged 47 years. Forty-seven days previous to examination, right abdominal, colicky and intermittent pain, developing slowly after meals, had been present. Later, vomiting and marked constipation developed. There was a mass in the ileocæcal region. Cholecystectomy for cholecystitis was performed. The cæcum was incised, and a submucous lipoma, about 5 centimeters in diameter, and covered by hyperæmic, thin, eroded mucosa, was removed. Cure was effected.

CASE 63. Kothney's case, 1919. The patient was aged 43 years. For 3 months the patient had had a cramp-like abdominal pain, appearing 1 to 1½ hours after meals, and reaching its greatest severity 2 to 2½ hours after meals. The pain was less intense if the bowels were loose. There was loss of weight. A tumor, about 10 centimeters in diameter, was found in the left lower quadrant of the abdomen. After taking a purgative, the patient passed a lipoma, 14 by 8 by 9 centimeters, covered with blood and mucus. An area, 10 by 5 centimeters, denuded of mucosa, which elsewhere was characteristic of the mucosa of the large bowel, was observed. Cure was effected.

CASE 64. Odelberg's case, 1921. The patient was a man, aged 48 years. Fifteen days before operation, chilliness, malaise, and diarrhœa had developed. The day before operation, pain in the right portion of the abdomen, vomiting, constipation, distention, and generalized abdominal tenderness had developed. There was muscle spasm of the right flank. An enema returned blood-stained. At laparotomy, intussusception was found. The ileum, cæcum, and ascending colon were resected, and an end-to-end anastomosis was performed. A submucous, pedunculated lipoma, 4 by 2.5 by 2 centimeters, was attached 30 centimeters above the valve. Recovery was effected.

CASE 65. Odelberg's case, 1921. The patient was a woman, aged 61 years. For the last 7 years, she had had violent attacks of right abdominal pain, accompanied by vomiting and diarrhœa. At laparotomy, an ileal intussusception, about 30 centimeters, was reduced. Resection was performed, and an end-to-end anastomosis was done. A yellow, elastic, submucous lipoma, 7.5 by 3.5 centimeters, protruded 1.5 centimeters externally. The serosa was thickened over the tumor (submucous and subserous). Recovery was effected.

CASE 66. Odelberg's case, 1921 (museum specimen). The tumors were three submucous, pedunculated lipomata of the jejunum, about 1.5 centimeters in diameter.

CASE 67. Odelberg's case, 1921 (museum specimen). The tumor was a submucous jejunal fibrolipoma, about 2 by 1 by 0.5 centimeter, with a pedicle 4 centimeters long.

CASE 68. Odelberg's case (necropsy record), 1921. A lipoma, about 2.5 by 2 by 1 centimeter, was attached to a diffusely fibrous and thickened mesosigmoid, by a twisted pedicle. Four pedunculated lipomata, varying in size from 2 by 1 by 0.5 centimeter to 2.5 by 2 by 1 centimeter, were attached to the omentum. There was also a pedunculated lipoma, about 1.5 centimeters in diameter, of the mesentery of the lower portion of the ileum, and a subperitoneal lipoma in the middle portion of the small intestine, bulging as much inside the lumen as outside. It was stated that the latter tumor was definitely submucous.

CASE 69. Dunet's case, 1921. A small submucous lipoma of the fourth part of the duodenum was encountered at necropsy in a case in which the patient had died of pulmonary tuberculosis. Symptoms of tumor had not been present.

CASE 70. Rinaldo's case, 1912. The patient was a man, aged 51 years. He had had recurrent attacks of constipation for years. During the last month, at each evacuation, protrusion of a bleeding, hard growth through the anus had occurred. It was replaceable by the fingers. Following physical effort, protrusion again occurred, and the growth could not be replaced. Later, the intestine came through the anus, causing intense pain and vomiting. A spheroidal, pedunculated tumor in the cylinder of the prolapsed and intussuscepted intestine was found at operation; extirpation of a submucous lipoma was performed. Laparotomy disclosed necrosis of the sigmoid. Resection and end-to-end anastomosis were done. Cure was effected.

CASE 71. Forster's case, 1921. The patient was a woman, aged 59 years. For the last 10 years, she had had increasingly frequent lower abdominal cramps. For

23 weeks, there had been vomiting, visible peristalsis, and an intermittently appearing tumor, about 8 centimeters in diameter, below the umbilicus. Laparotomy disclosed a tumor about 10 centimeters in diameter, in the transverse colon. Ileocolostomy was performed. Twenty-seven days later, resection of 30 centimeters of colon was done, and a submucous lipoma, covered by normal mucosa, was removed. Recovery was effected.

CASE 72. Forster's case, 1921. The patient was a man, aged 48 years. He had always suffered from abdominal pain and distention. There had been a sudden onset of generalized severe abdominal pain, accompanied by distention and vomiting. Flatus was not passed. A diagnosis of invagination or obstruction by a band of adhesions, and ileus was made. Laparotomy disclosed invagination of the ileum into the ascending colon. Disinvagination was done, and a smooth lipoma, 3 by 2 by 1 centimeter, 30 centimeters proximal to the ileocæcal valve, at a point of mesentery attachment, was excised. The muscular layer was absent. A tumor protruded into and external to the lumen of the bowel. It was both submucous and subserous, and there was infiltration with leucocytes and erythrocytes. Cure was effected.

CASE 73. Deroque and Deroque's case, 1924. The patient was a woman, aged 30 years. For 6 years, there had been intermittent abdominal pain, worse on the left side, and severe enough for the patient to remain in bed. Forty-two days before examination, she had had severe attacks of ileal pain, usually in the right side, but sometimes in the left side. Morphine was necessary. Laparotomy disclosed appendicitis and a vascular cæcum. Appendectomy was performed. A lipoma, about 5 centimeters in diameter, covered by normal mucous membrane, and attached posteriorly near the appendiceal orifice by a base about 3 centimeters in diameter, was found in the cæcum, and was removed by sectioning the base of the implantation. Cure was effected.

CASE 74. Carlucci's case, 1921. The patient was a woman, aged 43 years. She had had progressively more severe attacks of abdominal pain during the last 3 months, which occurred every 4 to 7 days. The pain was more severe in the right lower quadrant of the abdomen, lasted 20 hours, and was relieved by movement of the bowel. Nausea, and, at the last, fæcal vomiting, occurred. Blood was found in the stool. There was moderate abdominal distention. Ileus was present. At operation, intussusception of the transverse colon into the sigmoid was found. Free fluid was present. Resection and side-to-side anastomosis were performed, and a pedunculated, encapsulated, lobulated lipoma, 9 by 8 centimeters, attached to the apex of the region of intussusception, was removed. Death resulted.

CASE 75. Carlucci's case, 1921. The patient was a man, aged 53 years. During the last month, he had had four or five attacks of umbilical pain daily, which lasted 4 to 5 seconds. Examination disclosed an oblong mass in the left portion of the abdomen. Blood was present in the stools. At operation, the cæcum and ileum were resected, and end-to-side anastomosis was performed. An encapsulated, nodular, submucous lipoma covered with mucous membrane, attached by a fibrous pedicle 3 centimeters long to the mesenteric border of the ileum and extending through the ileocæcal valve into the cæcum, was removed. Cure was effected.

CASE 76. Chalier and Dunet's case (13, 14), 1921. The patient was a man, aged 46 years. Five days previous to examination, severe pain had occurred in the left lower quadrant of the abdomen, and symptoms of acute obstruction were present. A diagnosis of volvulus of the sigmoid was made. Operation disclosed a distended and hypertrophied sigmoid, the result of adhesions. There was an intussusception in the descending colon just below the splenic flexure. The colon was incised, and a pedicle of a submucous lipoma, about 5 by 3 by 3 centimeters, was amputated. There was necrosis of the mucosa at the free end of the tumor. The termination was not stated.

CASE 77. Vaccari's case, 1923. The patient was a man, aged 60 years. Four days before examination, intermittent, severe pain of the right lower portion of the abdomen had occurred. The pain radiated over the entire abdomen, especially to the umbilicus, and was accompanied by nausea, vomiting, and, later, hiccough. Two liquid stools were passed soon after onset of the pain, but no further passage of fæces or gas occurred. There was slight distention, moderate rigidity, and tenderness. At laparotomy, ileal intussusception was found. Ileocolostomy and resection of a pedunculated submucous lipoma, about 2 centimeters in diameter, covered by necrotic mucous membrane, and attached near the apex of the intussusception, was performed. On the external surface was found a small, bilobate, subserous lipoma, at the point of attachment of the peduncle of the submucous lipoma, and near the insertion of the mesentery. The muscle layers were intact, separating the points of origin of the pedicles. General peritonitis and death followed.

CASE 78. Degener's case, 1925. The patient was a man. For 8 years, at long intervals, blood had been present in the stools. At operation a submucous lipoma, 4 by 3 by 1 centimeter, was found in the duodenum. A scar at the apex of the tumor was assumed to be the site of healed ulceration and the source of bleeding.

CASE 79. Verger and Massias' case, 1922. The subject was a woman, aged 58 years. During the last month she had had anorexia, nausea, and diarrhœa. Free hydrochloric acid was absent. There was irregularity of the contour of the upper part of the pylorus. Necropsy revealed cirrhosis of the liver, and probably early carcinoma at the pylorus, also a submucous, sessile lipoma, about 1.5 centimeters in diameter, on the greater curvature of the stomach, 5 centimeters above the polorus.

CASE 80. Nash's case, 1924. The patient was a woman, aged 61 years. Six months previous to examination she had had an attack of diarrhœa followed by attacks of abdominal pain and severe constipation. One week previously, severe colicky pain and vomiting had occurred. Tenderness and rigidity were present in the right lower quadrant of the abdomen. At operation, the appendix was found to be thickened but not inflamed; the cæcum felt like a mass of worms. When it was incised, a submucous lipoma, measuring 10 by 6.25 centimeters, projecting from the posterior wall, was shelled out. Cure was effected.

CASE 81. Kaufmann's case, 1922. The subject was a woman, aged 72 years. Necropsy revealed a pedunculated lipoma of the transverse colon.

CASE 82. Kaufmann's case, 1922. The subject was a woman, aged 62 years. Necropsy revealed a pedunculated lipoma of the ascending colon.

CASE 83. Dittrich's case, 1924. A specimen was presented of a submucous lipoma of the ascending colon, causing intussusception and chronic ileus. Resection of the ascending and transverse colon had been performed in Kuttner's clinic. Recovery was effected.

CASE 84. Vogeler's case, 1924. The patient was a woman, aged 67 years. She had had constipation for many years. Recently it had become severe and was accompanied by a sense of obstruction and severe pain with movements of the bowel. Two days before admission, severe pain and vomiting had occurred. Proctoscopic examination revealed an obstruction and a movable,

bluish-red, tender tumor, about 10 centimeters in diameter, which bled easily and was situated above the anus. A diagnosis was made of torsion of the pedicle of the tumor. Four days later the tumor was passed spontaneously. It was a grayish, infarcted, necrotic, hæmorrhagic fibrolipoma.

CASE 85. Partsch's case, 1924. The patient was a man, aged 59 years. Three months previously, there had been an extrusion of a round lump from the anus by forceful action of the bowel. Spontaneous replacement had occurred. Ten days previously, there had been reappearance of the tumor. It was irreducible. Stools were thin and their passage was painful. Examination disclosed a dark brown, firm, nodular, encrusted, and dry tumor, about 10 centimeters in diameter, which smelled foul and was attached by a pedicle 8 centimeters above the anus on the right lateral wall. The tumor was drawn out; the pedicle was ligated and cut by cautery. Cure was effected.

CASE 86. Staemmler's case, 1924. The subject was a man, aged 40 years. A submucous pedunculated lipoma of the duodenum, attached near the papilla of Vater, was found. There was a second lipoma, attached to the free border of a fold of the mucosa, situated 0.75 centimeter from the first lipoma.

CASE 87. Swanson's case, 1924. The patient was a man, aged 59 years. He had had epigastric pain of 9 months' duration. The pain shifted to the right or left hypochondrium. At first it was dull; later it was acute and stabbing. A movable tumor was noted 2 months previously. There was relief of pain with disappearance of the tumor. Laparotomy disclosed 10 centimeters of ileum invaginated through the ileocæcal valve; there was invagination of the valve, ileum and cæcum into the ascending colon. Reduction of the invagination was accomplished, and a submucous fibrolipoma, 3.7 by 4.2 centimeters, attached by a 2 centimeter circular base on the antimesenteric border, was resected, and end-to-end anastomosis was performed. Recovery was effected.

CASE 88. Belz' case, 1925. The sex and age of the patient were not given. A presumptive diagnosis was made of partial ileus from adhesions. At laparotomy, the cæcum and ascending colon were resected, and a submucous lipoma, about 8 centimeters in diameter, of the ascending colon, was removed. An uneventful convalescence followed.

CASE 89. Tanasescu and Barbilian's case, 1926. The patient was a man, aged 54 years. He had had constipation alternating with diarrhœa, flatulence, and distress after meals over a long period of years. There had been recurring attacks of umbilical pain and passage of gas, but no fæces. Examination disclosed visible peristalsis and a rounded, firm, elongated mass appearing and disappearing. Roentgen-ray examination, 6 hours after a barium meal, revealed the colon filled to the sigmoid; the proximal portion of the transverse colon was narrowed and had an irregularly dentated border. At operation, intussusception of the transverse colon was found. Disinvagination, resection of a movable tumor, and end-to-end anastomosis were performed. A submucous lipoma, about 10 centimeters in diameter, soft and lobulated, attached at the mesocolic border by a base 4 by 6 centimeters and covered with normal mucosa except for a small, ulcerated area, was removed. Cure was effected.

CASE 90. Viannay's case, 1926. The patient was a woman, aged 38 years. She had had rectal bleeding for 4 months, with recurrent expulsion from the anus of a round tumor, about 4 centimeters in diameter. For 2 months tenesmus and a frequent desire to defæcate had been present. At laparotomy, intussusception of the sigmoid into the rectum was reduced. The sigmoid was incised and submucous enucleation of a solid, non-pedunculated submucous lipoma was performed. Cure was effected.

CASE 91. Heinonen's case, 1926. The patient was a woman, aged 35 years. She had had pain and diarrhœa for 6 weeks. Later, vomiting and abdominal distention and tenderness had developed. At laparotomy, disinvagination of 8 centimeters of intussusception was performed. A round, firm, submucous lipoma, 3.2 by 3 by 2.5 centimeters, attached at the mesenteric border by a pedicle 2.5 centimeters long, was excised.

CASE 92. Latouche's case, 1926. The patient was a man, aged 38 years. He had had recurring attacks of diarrhœa and vomiting. Three days previous to admission, he had had generalized paroxysmal abdominal pain and vomiting, which required morphine. There had been no flatus or movement of the bowel. A diagnosis was made of a ruptured appendix. Laparotomy disclosed free fluid in the peritoneal cavity. The appendix was normal. The cæcum was grayish-green. Non-reducible ileocæcal intussusception was found. Lateral entero-anastomosis and resection was performed. A pedunculated, rounded, necrotic tumor, about 4 by 3 by 3 centimeters, at the apex of the intussusception, was found. It was composed largely of fat containing areas of connective tissue, polymorphonuclear leucocytes, and hæmorrhage, and was probably a fibrolipoma. Death resulted from embolism.

CASE 93. Weicker's case, 1928. The patient was a man, aged 60 years. He had had pain on pressure in the left side of the epigastrium, which was worse when the stomach was empty. There had been occasional vomiting and diarrhœa. A test meal showed absence of blood and free hydrochloric acid. Roentgen-ray examination disclosed a tumor of the greater curvature. At operation, the stomach was incised, and a spherical, sessile, submucous lipoma, about 8 centimeters in diameter, on the middle third of the posterior wall near the greater curvature, was extirpated. Cure was effected.

CASE 94. Douglas' case, 1926. The patient was a woman, aged 41 years. She had had pain in the lower portion of the abdomen, constipation, and intermittent abdominal distention. There was a mass in the left inguinal region. A filling defect in the sigmoid was present. Sixteen centimeters of the sigmoid was resected, and end-to-end anastomosis was performed. The tumor was a submucous lipoma; the mucosa was ulcerated. Cure was effected.

CASE 95. Polak's case, 1928. The patient was a woman, aged 43 years. She had had severe abdominal pain 3 weeks previous to admission. Intermittent pain and vomiting had persisted. Ten to 12 centimeters of the ileum was invaginated 50 to 60 centimeters above the ileocæcal valve. Disinvagination was accomplished, and a submucous lipoma, about 2 centimeters in diameter, attached by a thick pedicle to the antimesenteric border, was extirpated. Recovery was effected.

CASE 96. Polak's case, 1928. The patient was a woman, aged 47 years. She complained of colicky pain of the right portion of the abdomen. A movable tumor was present. The cæcum and ascending colon were resected and ileocolostomy was performed. A pedunculated lipoma, about 8 centimeters in diameter, covered by necrotic mucous membrane, and attached to the hypertrophied wall of the ascending colon, was removed. Recovery was effected.

### GENERAL COMMENT ON THE ONE HUNDRED AND EIGHTY-ONE CASES KNOWN TO HAVE OCCURRED

Doubtless the reader has noted that the last abstract of a report of a case is numbered 96.

TABLE I.—SITUATION OF GASTRO-INTESTINAL LIPOMATA WITH RESPECT TO PRODUCTION OF SYMPTOMS

| Situation | With Symptoms | Without Symptoms | Total |
|---|---|---|---|
| Stomach | 5 | 17 | 22 |
| Duodenum (definitely) | 1 | 12 | 13 |
| Duodenum (probably) | 2 | .. | 2 |
| Jejunum (definitely) | 2 | 9 | 11 |
| Ileum (definitely) | 25 | 9 | 34 |
| Small intestine (not further localized) | 4 | 1 | 5 |
| Total small intestine | 34 | 31 | 65 |
| Ileocæcal valve only | 2 | .. | 2 |
| Ileocæcal valve, cæcum, and ascending colon (multiple) | ... | 1 | 1 |
| Ileocæcal valve and ascending colon (multiple) | ... | 2 | 2 |
| Ileocæcal valve and sigmoid (multiple) | ... | 1 | 1 |
| Cæcum only | 12 | 4 | 16 |
| Cæcum and ascending colon (multiple) | 1 | .. | 1 |
| Ascending colon only | 11 | 3 | 14 |
| Hepatic flexure only | 2 | .. | 2 |
| Transverse colon only | 9 | 1 | 10 |
| Descending colon only | 7 | .. | 7 |
| Descending colon and sigmoid (multiple) | ... | 1 | 1 |
| Sigmoid only | 11 | 1 | 12 |
| Probably sigmoid only | 2 | .. | 2 |
| Colon only | 4 | 2 | 6 |
| Probably colon only | 5 | .. | 5 |
| Throughout entire colon (multiple) | ... | 1 | 1 |
| Rectum only | 8 | 1 | 9 |
| Total large intestine | 74 | 18 | 92 |
| Apparently intestinal (data insufficient) | 1 | 1 | 2 |
| Grand total | 114 | 67 | 181 |

The 85 cases which represent the difference between 96 and 181 are accounted for in the articles by Stetten and by White and Judd, to which reference has been made.

*Incidence.* Benign neoplasms of the gastro-intestinal tract are comparatively rare. Eusterman and Senty found records indicating that 1.3 per cent of new-growths of the stomach for which operation was done at The Mayo Clinic between the years 1907 and 1921 were benign. A similar small percentage in all probability would obtain for benign new-growths of the entire gastro-intestinal tract, and of these, submucous lipomata form a small subdivision. Thus, Staemmler reported the occurrence of 116 adenomatous polyps and only 9 lipomata and 9 myomata of the small and large intestine, among 17,000 postmortem examinations. Staemmler also reported finding reports of cases of 88 myomata, 103 lipomata, and 26 fibromata and myxomata. The number of reported cases of lymphangiomata and hæmangiomata is much smaller. Helvestine, in 1923, found reports of 14 hæmangiomata of the small and large bowel. It appears that lipomata occur in approximately the same frequency as myomata, that they are next to the adenomatous polyps in frequency, and that they are considerably more common than fibromata, myxomata, hæmangiomata, and lymphangiomata of the small and large bowel.

Lipomata of the stomach appear to be equally as uncommon as those of the small and large bowel. Balfour and Henderson, in their series of 58 benign neoplasms of the stomach, did not find a lipoma.

The incidence of lipomata found at necropsy varies. In the series seen at The Mayo Clinic, 24 submucous gastro-intestinal lipomata were found in 3,924 consecutive necropsies, an incidence of 0.6 per cent. Twenty of these were situated in the small or large intestine, an incidence of 0.5 per cent, which is somewhat larger than the incidence of 0.05 per cent which Staemmler found in 17,000 cases. Again, Eliason and Wright found only one lipoma of the stomach in 8,000 necropsies, whereas the records of the clinic show 4 in 3,924 necropsies, a frequency approximately eight times greater than that of Eliason and Wright. With more careful examination than is usually accorded the small and large bowel, the reported incidence will increase.

It has been stated that lipomata of the stomach are less common than those of the small and large bowel. That only 5 of the 114 lipomata which produced symptoms, or 22 of the total of 181, were situated in the stomach bears this out. On the contrary, it does not follow that the tendency to formation of lipomata is less in the stomach than in the intestines. If there existed some means of comparing the unit areas of mucosal surface in the stomach with that in the intestines, it probably would be found that lipomata for a unit area of mucosa in the stomach are as numerous as lipomata for a unit area in the intestines.

A study of Table I reveals some additional interesting facts in regard to the incidence of lipomata in the various parts of the gastro-intestinal tract. Lipomata are about half again as common in the large as in the small intestine; lipomata which produce symptoms are about twice as common in the large as in the small intestine. Apparently lipomas are more common in the small bowel in those cases in which they are discovered incidentally at necropsy or at operation. However, in the series in which they were discovered at necropsy in the clinic, they were equally divided between small and large bowel. Lipomata in the small intestine are most

common in the ileum, and least common in the jejunum; in the large intestine, they are most common in the cæcum and ascending colon and next most common in the sigmoid. Sixteen of the 35 ileal lipomata were situated within 75 centimeters of the ileocæcal valve, and very few of the remaining lipomata definitely were in the upper part of the ileum. It seems that lipomata tend to occur more commonly in those segments of the gastro-intestinal tract composed of the stomach and duodenum, and of the lower part of the ileum, cæcum, and ascending colon. In the stomach, moreover, the majority are situated in the distal half. If this grouping in the segments of the gastro-intestinal tract bordering its distinct anatomical divisions, the pylorus and the ileocæcal valve, has any significance, it is not apparent. However, it invites speculation as to whether some physiological characteristic of these portions of the gastro-intestinal tract favors formation of lipoma.

This distribution varies from that found by Virchow, who stated that lipomata are more common in the stomach and upper parts of the small intestine. It differs also from that described by Nothnagel, who claimed that their favorite site was the rectum or lower part of the ileum, or that by Stetten, who found them about equally divided between small and large bowel.

The cases were about equally divided between the sexes; there were 81 in males and 72 in females among the 155 cases in which sex was mentioned.

Table II gives the ages at which the lipoma was found at operation or at necropsy. Seventy-two per cent of the 101 lipomata which produced symptoms and 76 per cent of the 149 lipomata, composed both of those which produced symptoms and those which did not produce symptoms, in cases in which the age of the patient was known, occurred after the age of 39 years, or within the so-called cancer age.

*Pathological anatomy.* Fat cells frequently were found in the submucosa of the gastro-intestinal tract (Fig. 7). In the material obtained at necropsy, which was available for study, the fat cells were discrete, occasionally were in groups, or were diffusely distributed. They were sometimes sufficient in number to give a yellowish tint to the mucosa, with or without the formation of small lipomata 3 to 4 millimeters in diameter or larger (Group 2, Cases 23, 24, 25, and 26). The fatty infiltration may be found in one region or in multiple regions, or it may be distributed diffusely. Whether lipomata are believed to be metaplastic, heterotopic, inflammatory, or neurosecretory in origin, the growth of these collections of fat cells into single lipomata, multiple lipomata (observed thirteen times), or diffuse lipomata (probably Knowlton's case represents this type), is easily visualized. In different instances, the process is demonstrable in all stages, from that of a small collection of cells in the submucosa (Fig. 7) to that of a large tumor.

TABLE II.—AGE OF INCIDENCE OF GASTRO-INTESTINAL LIPOMATA WITH RESPECT TO PRODUCTION OF SYMPTOMS

| Age, Years | Causing Symptoms | Not Causing Symptoms | Total |
|---|---|---|---|
| Under 20 | 2 | 1 | 3 |
| 20 to 29 | 5 | 3 | 8 |
| 30 to 39 | 21 | 2 | 23 |
| 40 to 49 | 29 | 4 | 33 |
| 50 to 59 | 27 | 9 | 36 |
| 60 to 69 | 14 | 19 | 33 |
| 70 to 79 | 2 | 7 | 9 |
| 80 to 89 | 1 | 3 | 4 |
| Not stated | 13 | 19 | 32 |
| Total | 114 | 67 | 181 |

The fat cells observed were of the adult type. No immature cells, such as those described by Staemmler, on the periphery of the small lipoma, were observed. The microscopic tumors were enclosed in the connective tissue of the submucosa. As the tumors increased in size, the line of demarcation between the submucosal connective tissue and the fat became more definite, and the development of the submucosal connective tissue into a thin or a comparatively thick capsule was accomplished. Even in the small tumors, septa dividing the tumor into lobules were seen. Such septa might be very fine or comparatively heavy. As the proportion of connective tissue increases, one is more inclined to apply the term fibrolipoma to the growths.

Arterioles and numerous capillaries, each with an amount of supporting stroma in proportion to the size of the vessel, were present. In the supporting stroma of the blood vessels, in the small, symptomless tumors, could be found occasional groups of three to five small, mononucleated cells, groups of cells which have been pointed to as evidence of the inflammatory origin of these tumors.

The mucosa was thinned and atrophic, or normal, in appearance. The muscularis mucosæ in the smaller tumors could be traced intact over the surface. In the larger tumors it became faint or unrecognizable.

The muscular layer in the smaller tumors was not obviously affected. In the larger sessile tumors, this layer was thinned, and the yellow

of the fat might be apparent externally, a point of importance in the recognition of these tumors at operation. In the smaller, sessile tumors, the mucosal and muscular layers seemed to be displaced about equally in the opposite directions (Fig. 6). As the tumors became larger, by virtue of the intra-intestinal pressure, the wall of the bowel was pushed outward, the serosa of the encircling wall came in contact with the serosa overlying the base of the tumor (Fig. 5), and the two serosal layers became adherent and separated the layers of muscle which seemingly had been enfolded, or pulled in by the drag of the tumor. Such infolding has been described in all three cases in Group 1 and in Case 20 in Group 2. This arrangement provides a possible explanation of the conditions observed in some of the cases, which leads to a description of the tumor as one arising in the muscular layer. Of the lipomata which caused symptoms, those of the small intestine were smaller than those of the large intestine as a rule. Most of the tumors which cause symptoms in the small intestine are about 4 centimeters in diameter, and a few are from 5 to 10 centimeters in diameter; those of the large intestine are usually from 5 to 10 centimeters in diameter, although sometimes they are smaller. Twenty-three lipomata were felt by abdominal palpation. The smaller size of those in the small bowel partially explains why only three were palpated. Of the symptomless tumors, the sizes noted vary from an almost microscopic swelling to about 1.5 centimeters in diameter. The size of the tumor, as well as its situation, seems to determine the time of the appearance of symptoms.

The shape varies with the type of attachment and size. If it is attached by a fibrous pedicle, the tumor may be oval, or it may be flattened and elongated. The pedicle varies markedly in length. If the lipoma is attached by a broad base, with the lipomatous structure separated from the muscularis only by the capsule, the tumor may vary in shape from that of a disk to that of a pear. They may have rounded and smooth, or irregular and lobulated surfaces.

The presence of a considerable amount of adipose tissue beneath the mucosa, in the fold of the ileocæcal valve, in Cases 23, 24, 25, and 26, of Group 2, which were observed at the clinic, is to be noted. It is an impression that such depositions of fat are not infrequently encountered at necropsy. A study of the sites of formation of adipose tissue in the various parts of the intestinal tract might reveal the ileocæcal valve to be a common one. However, only two clinical cases of lipoma of the ileocæcal valve have been recorded; one (reported by Brouwer) was a pedunculated tumor attached to the valve; the other (reported by Compton) was a diffuse thickening comparable to that in Group 2.

Submucous lipomata were associated with subserous lipomata in 7 instances in this series. They were attached at the same or different points of the wall of the bowel, and might both be sessile and pedunculated, or one might be pedunculated and the other sessile. There might be multiple tumors of both types in the same case. The muscle layer may be intact (Vaccari) or partially destroyed so that the tumors are continuous (Forster). In the latter instance an intramuscular origin may be postulated.

If a lipoma is of sufficient size, it leads to the development of associated anatomical, pathological, and physiologico-pathological conditions: irregular and forceful peristalsis, obstruction at the pylorus and of the intestine; ulceration; intussusception, which no doubt is preceded in many instances by dimpling of the wall of the bowel; spontaneous expulsion, and circulatory changes, results of pressure incidental to forceful peristalsis or intussusception. The tumor itself may be traumatized by a foreign body, with ensuing ulceration. The healed scar in Degener's case may have been the result of such trauma, although that an ulcer might occur on a lipoma, as well as any other ulcer might occur in the duodenum, must be considered. The healed scar in Case 3, Group 1, similarly could have been due to external trauma or to internal hæmorrhage.

Intussusception occurred 26 times as a complication in the 29 cases of lipoma of the small bowel in which data on this point were available. In the large bowel it occurred in 33 of 62 cases. The intussusception accounted for 24 of the 47 abdominal tumors that were palpated in the 114 cases with symptoms. The apex of the intussusception reached a point low enough for the tumor (usually attached to the apex), that grew from the wall of the sigmoid or higher segment of the bowel, to be palpated by the examining finger or to be extruded from the anus, in 14 instances. In the case of this sort, which Stetten recorded, the tumor was ileal; in the majority of instances, the tumor was attached to the sigmoid or descending colon. Eight rectal tumors lent themselves to examination by the finger or, after extrusion, to inspection by the naked eye. Spontaneous expulsion occurred 12 times. It is to be noted that this has occurred in only 2 cases (45, 84) since 1909. Early diagnosis and

surgical interference probably accounts for the recent rarity of this complication.

Interference with the circulation of these tumors leads to œdema, congestion, ulceration, hæmorrhage into the substance of the tumor, infiltration with leucocytes, and necrosis. The mucosa may be completely or partially absent, necrotic or ulcerated. These changes may lead to marked swelling of the tumor, as illustrated in the difference in size of the tumor at the first and second stages of resection in Case 3, Group 2. This offers an explanation for obstructive symptoms not explainable on the basis of size of the tumor. Cystic degeneration of the tumor has been described. Hæmorrhage from the tumor or from the wall of the bowel, congested and necrotic by virtue of the process of intussusception, explains the presence of the blood so frequently reported in the stools.

*Symptoms.* Balfour and Henderson have pointed out that benign tumors of the stomach are symptomless unless complicated by bleeding, ulceration, or intermittent obstruction at the pylorus, or unless there is interference with gastric motility and secretion due to the size and extent of the tumor. The 5 cases of gastric lipoma causing symptoms which have been recorded indicate that this is true of gastric lipomata as well as of other types of benign tumor of the stomach. In Fischer's case, the symptoms were those of ulcer, hæmorrhage, and tetany. The chief complaint in Spitzmueller's case was pain brought on by exercise and excitement, and the palpable tumor. The description of the pain suggests angina so strongly that the relief by operation causes some astonishment. The lipoma reported by Randisi definitely produced pyloric obstruction, probably of the ball-valve type. The distress in the left portion of the epigastrium, which was worse when the stomach was empty, the occasional vomiting, and the frequent diarrhœa in Weicker's case can be explained by disturbances of motility due to the large size of the tumor. Repeated hæmorrhage and vague symptoms like those of ulcer in White and Judd's case were obviously due to the ulceration on the surface of the tumor. In addition are the 2 cases which came to necropsy, reported by Bénaky, and in which pyloric obstruction evidently had been produced, and the case reported by Nahmmacher, in which there was a depressed scar on the surface of the lipoma, suggesting the possibility of previous hæmorrhage.

Stetten assumed that the lipomata passed spontaneously in the cases of Lewtas and Ward were of duodenal origin. Biliary colic was simulated in these 2 cases. Degener reasonably assumed the site of a healed ulceration in the mucosa of a lipoma to be the source of recurrent melæna. In a postmortem examination reported by Nattan, Larrier, and Roux, a duodenal lipoma, the diameters of which measured 6 and 3 centimeters, was associated with dilation of the stomach. The absence of proved cases of lipoma of the duodenum which produced symptoms relegates a consideration of such symptoms to the field of speculation. However, the cases of Lewtas, of Ward, of Degener, and of Nattan, Larrier, and Roux, as well as analogous cases of benign tumors of other types, makes it more than probable that hæmorrhage, pain, symptoms of obstruction, and even ulcer syndromes of a sort, in time will occur in cases of lipoma of the duodenum.

Various authors have attempted a classification of the symptoms of submucous lipoma of the intestinal tract. However, a review of the cases herein reported and of the abstracts of the 111 clinical cases hitherto reported fails to reveal any syndrome peculiar to the lipoma. The symptoms are those of intestinal obstruction. The obstruction exists by virtue of the tumor encroaching on the lumen of the bowel (Cases 2 and 3, Group 1), or by virtue of intussusception (Case 1, Group 1). All varieties of intestinal obstruction are encountered: acute, subacute, chronic, chronic or subacute with exacerbations, partial or complete, progressive or intermittent, and so on. The actual onset of symptoms of obstruction may be preceded by months and years of gastric and abdominal symptoms too slight to induce the patient to seek relief, and too vague to point the way to a diagnosis. The occurrence of the pain at certain hours after meals may suggest peptic ulcer. Appendicitis is simulated especially by the cæcal lipomata.

*Diagnosis.* A diagnosis of submucous lipoma of the gastro-intestinal tract will be made rarely. In the stomach, the lipoma may be identified as a benign tumor. The history does not often assist in the differentiation of benign and malignant lesions. Roentgenology now furnishes the best means of diagnosis of benign tumors. Balfour and Henderson found that in their series of benign tumors of the stomach, 40 per cent were reported by the roentgenologist as benign. Moore has pointed out the roentgenological signs of benign tumor which distinguish it from malignant tumor. There seems, however, to be no method by means of which the lipoma may be distinguished from the other benign lesions of the stomach.

The same difficulty, although a greater one, exists in the small and large bowel. There the clinician will be content, through necessity, with a diagnosis of an obstructing lesion of the small or large bowel. In every case, reviewed from the literature, with the exception of those in which the growth was seen on examination by rectum, the clinician probably has encountered the same difficulty in reaching a diagnosis which was encountered at the clinic. An attempt may be made to establish whether the lesion is malignant or benign. The long duration of symptoms, as in the cases of Tromp, Braun, and Forster, or the finding by roentgenological methods of a polypoid lesion, may suggest a benign tumor. However, the most common benign polypoid lesion of the colon is the adenomatous polyp; its marked tendency to malignant degeneration renders valueless the assumption that a polypoid lesion is benign. The occurrence of 72 per cent of the lipomata in patients of cancer age, the frequently associated loss of weight, and the frequent appearance of blood in the stools do not aid in the attempt to establish the polypoid lesion as a benign neoplasm. If the tumor can be established as being benign, a lipoma may be thought of, especially, as Albrecht suggested, if the patient is obese or if lipomata are present elsewhere. Meyer mentioned that a soft tumor palpated through the abdominal wall suggests a lipoma. The value of the point is doubtful.

Only when a tumor is rectal, or when it prolapses into the rectum or through the anus, will it be possible to make a definite pathological diagnosis. The following characteristics will point to the nature of the tumor: softness and lobulation of the tumor, elicited by palpation; the yellowish tinge of the mucosa or of the area of surface denuded of mucosa, when the growth is seen externally or through the proctoscope, will point to the nature of the tumor. However, the changes secondary to circulatory disturbances may so alter the lipomatous consistence, color, and structure that recognition of the condition would be impossible even with the aid of biopsy.

At operation the benign character of the growth has been suspected because of the consistence of the tumor, its pear-shape, its broad base of attachment, and its yellow appearance as seen through the muscle covering its base. In some instances, excision instead of resection has been carried out, with reduced risk to the patient.

SUMMARY

Three submucous lipomata of the colon which produced symptoms, and which were removed surgically, and 25 which did not produce symptoms and were found incidentally at operation or necropsy, have been presented from the records of The Mayo Clinic.

Abstracts of reports of 68 cases previously reported and not included by Stetten or by White and Judd are given.

A total of 181 submucous lipomata are available for study. Of these, 114 produced symptoms and 67 did not produce symptoms.

Submucous lipomata form one of the more important subdivisions of benign gastro-intestinal neoplasms. Clinically, they rank in frequency with myomata, are less common than the adenomatous polyp, and more common than the other types of tumor in the small and large bowel; in the stomach, they are apparently among the least common of benign neoplasms.

They seem to occur more commonly in the stomach and duodenum, and in the lower part of the ileum, the cæcum, and the ascending colon, and twice as commonly in the large as in the small intestine.

They occur singly or multiply, sessile or pedunculated, in association with the subserous variety, and equally as commonly in male and female.

The symptoms are those of irregularity in force and rhythm of peristalsis, obstruction of the stomach, especially at the pylorus, and of the small and large bowel, intussusception, and ulceration incidental to the circulatory changes wrought by pressure and intussusception or caused by external trauma.

The diagnosis of a lipoma of the gastro-intestinal tract has been made before operation only in exceptional instances; the diagnosis usually cannot be more accurate than that of benign tumor.

A definite diagnosis of lipoma can be made only under certain conditions: (1) when the tumor can be seen through the proctoscope or after it has prolapsed externally, and the appearance then is typical, and (2) when biopsy can be made from a rectal lipoma or from a lipoma attached to the apex of an area of intussusception which prolapses into the rectum.

The occurrence in patients who are within the cancer age, of 72 per cent of the lipomata which produce symptoms, as well as the often short duration of symptoms of loss of weight and blood in the stools may readily suggest the presence of a malignant process.

The consistence, the shape, the broad base of attachment, and the yellow of the fat shining through the muscular layer may in some instances suggest the character of the tumor to the operator.

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# EDITORIALS


## SURGERY, GYNECOLOGY AND OBSTETRICS

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## THE MEDICAL TREATMENT OF CANCER

As Lord Moynihan has tersely stated, cancer is a dirty fighter, and one out of every seven persons aged more than thirty-five years dies of the disease. If for the moment we disregard those patients who are operated on for cancer early in the course of the disease, or those who are cured by radiotherapy, we may say, with regard to the average of the population, that 10 per cent have cancer and 90 per cent do not. Cancer never develops in sound tissue. And as the evidence available, both clinical and experimental, is analyzed, there is a strengthening conviction that cancer is not caused by some influence outside the body but by changes that take place within the body, and that the 90 per cent of persons are sufficiently well protected against the ordinary local disturbances which may produce cancer, if they are susceptible, to prevent the disease. We must assume that such protection through natural resistance is not always of the same degree because whereas the disease may develop after a brief precancerous phase in certain persons who are extremely susceptible, it may develop in others only after a prolonged stage of chronic irritation.

Broders' classification of cancer, based on the criteria established by the early work of Wilson and MacCarty, makes possible a graphic conception of the disease. The less malignant types in Broders' classification, grades 1 and 2, may indicate higher resistance, and the more severe types, grades 3 and 4, lower resistance, rather than that the severity of the disease indicates a difference in the causes which led to it. If we had some way of measuring the resistance of the individual to cancer, it might even be possible to look forward to the time when low resistance could be raised.

Growing embryonic cells of the chorionic villi (Langhan's cells) resemble malignant cells in rapidity of division and growth. The cancer cell, notwithstanding its power of rapid growth, lacks the strong heredity of the Langhan's cells, and is much more susceptible than the normal cell to destructive influences. If we analyze cases of cancer clinically, we find that the chief causes of pain and distress are the involvement of nerves, interference with the function of a viscus, and infections due to the breaking down of cancerous tissue.

It has long been known that cancer in a relatively sterile situation, which does not involve nerves and has room for expansion without serious pressure on other organs, for instance, cancer in the liver, can grow to great size without causing the patient much discomfort. Other things being equal, if a patient has an early cancer of an organ, for instance of the rectum, threatening as it does

painful death from involvement of the bladder and genitalia, and infection, if the growth can be removed without too much risk, it should be done even in the presence of incurable secondary involvement elsewhere in the body. The life of the patient will thus not only be prolonged but made more bearable during the terminal stages.

One of the methods by which the body offers resistance to cancer is encapsulation of the cancer cells in connective tissue, which acts as a protective mechanism to prevent further spread. The cancer cells, however, may remain for years in such hibernation, only to break loose at some future time.

It has been suggested, especially by those who work with pulmonary tuberculosis, that if the primary lesion can be removed, the secondary growth often is delayed in its activity by an immunizing process, an increased resistance of the patient's protective mechanism, and perhaps this is as true of cancer as of tuberculosis.

In speaking of the medical treatment of cancer, therefore, one is not thinking of cure but of those measures of palliation which may aid in increasing resistance as well as bringing about destruction of the cancer cell. Are we prepared to say that there are no medicaments that will delay the progress of cancer or increase the resistance of the patient who already has the disease?

Arsenic given internally was believed at one time to increase resistance and delay the growth of cancer. The use of colloidal lead and colloidal gold by skilled observers has appeared to have some such effect. What we need is a survey of these possible methods of giving relief to see whether there are means of increasing the resistance of the patient to the disease, and at the same time a survey of the effects of surgery, radiotherapy, and any or all agents which in the past or in the present have the reputation of being valuable in the treatment of cancer. Although the medical profession looks with skepticism on any unscientific form of treatment of cancer it is sufficiently open minded to view without prejudice any form of treatment which may have value.

W. J. MAYO.

## POSTOPERATIVE LUNG COMPLICATIONS

WITH the steady decline in the mortality and morbidity following surgical operations, the importance of postoperative lung complications tends to increase, since on the whole they have not diminished in the same ratio. These conditions should be thought of as postoperative rather than postanæsthetic since it is quite clear that they, at least, are not entirely due to the anæsthetic though undoubtedly anæsthesia is a factor, sometimes the important factor. It is probably true that such complications are more common after the use of ether, but it is quite certain that they occur no matter what anæsthetic is used and that they are not uncommon where the anæsthetic has been regional or even local in type. It is notable that they are more common and more severe in connection with abdominal operations and particularly operations upon the upper abdomen. The incidence following operations upon the chest wall or the lung itself should not properly be included. Despite the large amount of work which has been devoted to the assignment of the various causative factors, there is as yet no general agreement. Among the causes certainly at times operating to cause these conditions may be listed (1) inhalation of irritating or foreign substances, (2) irritation from the anæsthetic itself probably most commonly associated with ether, (3) emboli, and finally (4) atelectasis, a cause which has commanded increasing

attention and which is probably a very important factor.

Atelectasis probably arises commonly from the following sequence of events. Mucus collects in the smaller bronchi, respiration is slowed, and its depth diminished sometimes by medication, sometimes by the anæsthetic, and finally, particularly in connection with operations on the upper abdomen, respiration is voluntarily restricted because of pain. Of these factors the slowing of respiration is becoming increasingly important in connection with some of the newer anæsthetic methods. Thus the administration of various of the barbituric acid derivatives, and the increasing use of spinal anæsthesia accompanied by pre-anæsthetic medication with morphine and other drugs tend to create a larger group of patients in whom respiration is slowed over a considerable period of time quite apart from the conditions incident to the operation. At least a good case has been made for the proposition that atelectasis is a very important factor in many of the postoperative lung complications and if this be true, it is of essential importance that it should be counteracted by appropriate means. Particularly the work of Henderson has shown that the administration of carbon dioxide will do much to relieve the early conditions leading to atelectasis. It is doubtful whether the importance of this work has been sufficiently generally recognized and whether the administration of carbon dioxide after surgical operations, and particularly in patients in whom there is any tendency to slowing of the respiration, is becoming a routine procedure. Many anæsthetists have made it a practice to conclude the inhalation anæsthesias with the administration of carbon dioxide and this is undoubtedly desirable. On the other hand, the conditions giving rise to atelectasis can probably not be done away with by a single administration of this kind. It is at least worth while to consider whether the routine administration of carbon dioxide two or three times in the twenty-four hours for the first two days following operation is not sufficiently desirable to be incorporated as a regular practice in our surgical routine. My own experience in the past year seems to indicate that the routine administration of carbon dioxide has very importantly diminished the number of postoperative lung complications and since the method is quite harmless and unobjectionable, a much wider adoption of the method would seem desirable. I incline to the view that the postoperative use of carbon dioxide is the most important single contribution to the ultimate safety of anæsthesia which has been made in many years.

HUGH CABOT.

# MASTER SURGEONS OF AMERICA

## WILLIAM GIBSON

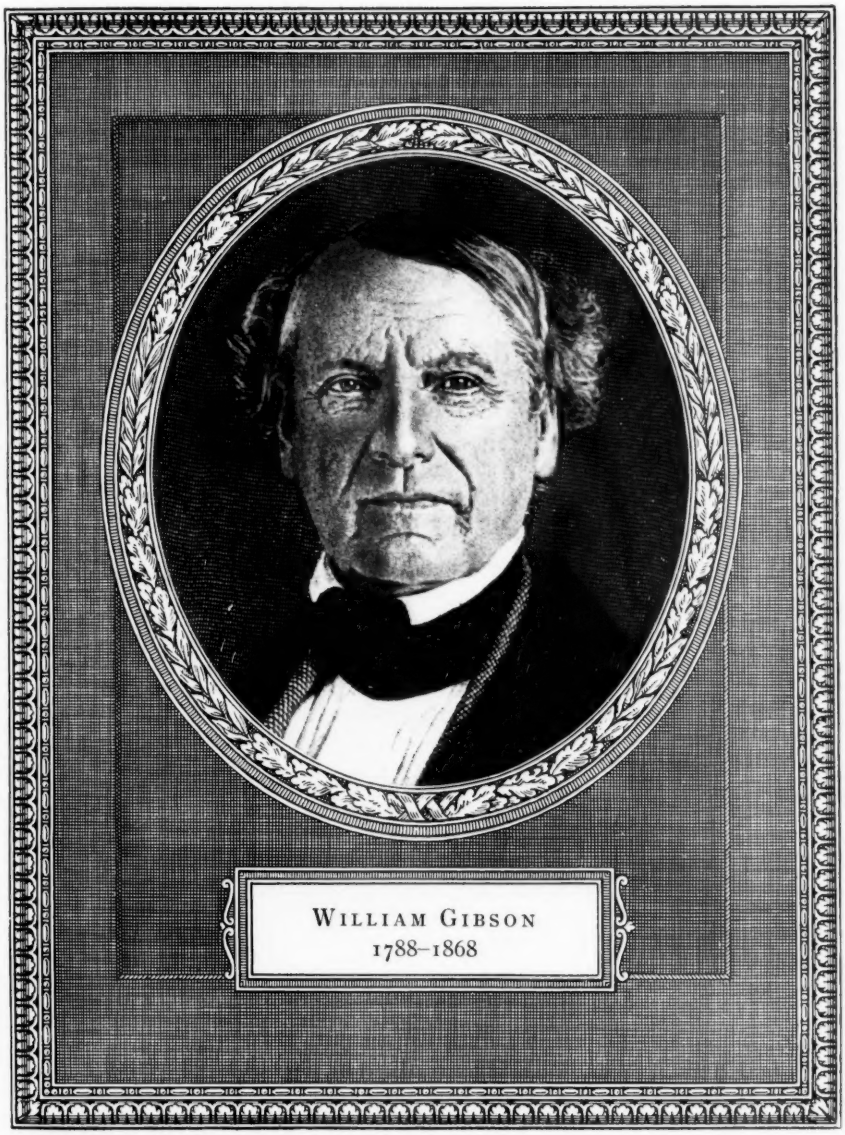
A GREAT teacher and a great surgeon was William Gibson. He was born in Baltimore, in 1788, and as his parents were well to do they were able to give him every educational advantage. As a youth he attended Annapolis College and later he entered the sophomore class at Princeton.

In the winter of 1806–1807 he attended the surgical lectures of Professor Physick in Philadelphia. Like other men of attainment, he early appreciated his own latent capacity. One day after Physick's lecture he seemed abstracted and thoughtful, and when questioned by his fellow students answered that he expected some time to succeed the great Physick. Thirteen years later this actually happened.

When the Physick lectures were concluded, Gibson sailed for Europe and entered the University of Edinburgh. His graduation thesis in Latin, "De Forma Ossium Genitilitæ," evoked favorable comment. Soon after he visited London and became a member of the household of Sir Charles Bell, for whom he conceived a profound admiration. He considered Astley Cooper great, but Bell even greater. Indeed, one of his sons was named Charles Bell and he subsequently became a distinguished surgeon. While in London, Gibson had the opportunity of seeing many of the wounded after the battle of Corunna. Some of his biographers state that receiving news of the impending battle he managed through influential friends to board a British transport and was present during the engagement.

In 1810 he returned to Baltimore. In 1811 he married for the first time, and by this marriage had five children, three sons and two daughters. By a second marriage he had two more daughters.

In 1812, during the riot in Baltimore, he saw a man fall from a gunshot wound in the groin. There was a profuse hæmorrhage which Gibson checked by digital compression. He then immediately obtained assistance, exposed and tied the common iliac artery, found that the distal end of the torn artery also bled, and closed two holes in the intestine. The wound was then held together with adhesive plaster, but the patient succumbed to peritonitis on the fifteenth day, from intestinal leakage. The lower extremity remained viable. This was the first demonstration of the establishment of collateral circulation of the lower extremity after ligation of the common iliac.



WILLIAM GIBSON
1788–1868

The same year Gibson operated on General Winfield Scott, who had been wounded at the battle of Lundy's Lane, near Niagara. Upon removal of the embedded bullet the persistent sinus in the leg healed.

About this time Gibson organized the medical department of the University of Maryland, and became the first professor of surgery in this school. In September, 1819, however, he was appointed to the chair of surgery at the University of Pennsylvania, which he occupied for thirty-six years. At this time his old friend Professor Physick, who because of ill-health had retired five years before after occupying the chair of surgery for twenty-seven years, was recalled to the chair of anatomy.

In 1824, Gibson's textbook, *The Principles of Surgery*, dedicated to Physick, made its first appearance. It was the standard work of its time and eventually ran through eight editions.

Gibson was the first to introduce systematic clinical instruction, always stressing the principles of his work. One of his biographers says: "He had a chaste, offhand style of lecturing. . . . If the eyes were shut it was like reading a book." He successfully performed a cæsarean operation twice on the same patient with complete recovery (1835–1837).

In 1811 he devised linear extraction of cataract. In 1818 he operated for strabismus, twenty-one years before Dieffenbach. He was the first to perform suprapubic lithotomy. He devised a circular saw actuated by clockwork, for the cutting of bones. He had the courage to report two cases of rupture of the axillary artery following attempted reduction of dislocated shoulders.

In the summer of 1839 Gibson again visited Europe and in 1841 this visit was described in a book of 390 pages, *Rambles in Europe in 1839*. This is a charming work with faithful descriptions of the great medical centers in London, Paris, Edinburgh, and Dublin. It is remarkable to note how little the essential spirit of these great centers has changed since that time. The notables of the period live and move across the scene as one reads the book.

Gibson's amusements were hunting, taxidermy, fishing, and carpentry. He was very fond of music and played the violin. For over sixty years he faithfully kept a journal, which reached the imposing number of 150 volumes. His accuracy was so well known that occasionally he and his journal were called upon to determine the exact date of some occurrence or the state of the weather on a certain day.

He was a man of strong character and equally strong prejudices. He was violently opposed to the use of tobacco and was once vice-president of the Anti-Tobacco Society of London. He repeatedly stated that he had added twenty years to his life by not smoking. He was an excellent observer and correctly stated that men got along more by tact than by talent. But he was not amiable. As an example, it is related that after twice warning a noisy young son at the

table to be quiet, he finally impaled the child's foot to the floor with the carving fork, remarking, "Now, will you be still?"

He was somewhat vain and on his return from his "Rambles in Europe" appeared before his class in a loud suit of shepherd's plaid, which occasioned much cheering from the students. This he took as personal acclaim, though it was really intended for his startling garb.

He was passionately fond of fishing. Indeed, it was while on one of his fishing trips, in his eightieth year, that he died, from what may be supposed to have been senile gangrene of the foot.

Years before, while on a fishing trip accompanied by a lawyer friend, he had an altercation with another man over a boat, and beat him up severely. His friend the lawyer defended him in the ensuing action brought against him and to Gibson's surprise rendered a bill for legal services, which was paid without comment. Shortly after another fishing trip was undertaken with the same legal companion, and as the result of some tartar emetic slyly added to the luncheon the lawyer became violently sick. He was attended by his medical friend, who then rendered his bill for an amount identical with that which had been charged by the lawyer.

William Gibson was one of the great figures of his time—a talented, energetic surgeon of great capacity, sound judgment, and clear vision. His literary ability was considerable. His qualities of intellectual honesty and energy greatly overbalanced any irascibility which he sometimes displayed. JOHN C. A. GERSTER

# THE SURGEON'S LIBRARY

## OLD MASTERPIECES IN SURGERY

ALFRED BROWN, M.D., F.A.C.S., OMAHA

### THE OLDEST SURGERY IN THE WORLD

EVER since surgical history has been written authors have harked back to Hippocrates and the ancient Greeks for the starting point of real surgery. Occasionally one more daring has gone back half a millennium or so further and pointed out the mention of surgical facts in the works of Homer. Beyond that, we, from our self appointed pinnacle of modernity, have considered and freely stated that all was mysticism, supernaturality, and belief in implantation of diseases by the gods with nothing but the recipe books of the magi and others to guide the poor benighted in their search for health.

We have felt so secure in this opinion that our ideas have become fixed and we have stated as facts matters which were actually only suppositions. In fact we are in a position where our whole conception of surgical history must be made over.

Professor Breasted with his translation of the Edwin Smith *Papyrus*[1] and its publication by the Chicago University Press compels us to discard all our previously held ideas and build for ourselves a new chronological conception of the development of surgery. Instead of Hippocrates being the originator of surgical method and surgical description he is, according to the time in which the author of the Smith *Papyrus* lived, actually as much of a modern to that surgeon as we are to him. Consequently we must move Hippocrates from the far background of our picture of surgical history and allow his place to be taken by this unnamed Egyptian surgeon meanwhile moving Hippocrates to the most prominent place in the middle distance.

If we make this change in our picture, and for the sake of truth, it must be made, how are we to fill in that space between the background and the middle distance? At present, save for the Assyro-Babylonian fragments; the few Egyptian recipe books; the record of the magnificent work of Moses along the line of sanitation and health prevention; and the ancient Indian works, if they antedate Hippocrates, and there is some doubt if they do, there is nothing except the surgical portion of the *Papyrus Ebers*, that can be used to fill in this period of twenty-five hundred years, and further discoveries must be awaited before any definite data can be obtained.

[1] The Edwin Smith Surgical Papyrus; Published in Facsimile Hieroglyphic Transliteration and Commentary. By James Henry Breasted. Vols. i and ii. Chicago: The University of Chicago Press, 1930.

In the meantime the Smith *Papyrus* furnished definite evidence that the general trend of surgical didacticism which has held the stage to the present was then, nearly five thousand years ago, an established method. The author of the original book was evidently a practicing and practical surgeon whose method of teaching was by the citation of case histories. In the fragment which constitutes the Smith *Papyrus* forty-eight cases are cited. These begin with cases of head injury and proceed downward toward the feet including in turn throat and neck; clavicle; humerus; sternum; overlying soft tissue and true ribs; shoulders; and upper spinal vertebræ. Here the manuscript stops and as Breasted puts it referring to the scribe who wrote the *Papyrus*, "One can imagine him yawning, rising indifferently and going home to his dinner, quite unconcerned, and altogether unaware of the fact that he was leaving the future civilized world entirely without any knowledge of his great ancestor's cases on the surgery of the internal organs, which in all likelihood followed immediately on that of the spine." In the *Papyrus* is found the arrangement of teaching material anatomically from head to foot which was so commonly used later and which in some textbooks of anatomy persists today.

The knowledge shown by this ancient surgeon was considerable. As examples: He describes paralysis of one side of the body following injury of the brain; and notes the shuffle of one foot after such an injury. He reduces a dislocation of the mandible by placing the thumbs on the jaw and forcing the condyloid processes back into position; and an extremely important fact is that he counts the pulse. That he was a scientific observer aside from a mere "healer" is shown by the fact that in sixteen of his examinations he advises against treatment, considering the case hopeless. In spite of this he takes enough interest in the diagnosis to note the symptoms and signs even though he prescribes nothing. He repeatedly advises his readers to let nature do the work and in this again precedes the Hippocratic ideas.

Students of surgery are greatly indebted to Professor Breasted for furnishing this most important work in readable form and students of medical history have now a tremendous task before them to fill in the gap left between Hippocrates and the unknown Egyptian surgeon who wrote a book which may have been the famous "Secret Book of the Physician" to which the *Papyrus Ebers* refers.

# REVIEWS OF NEW BOOKS

DURING the past decade, few fields of medicine have been as thoroughly investigated as that of the stomach. The reports of physiological investigations, clinical studies, and various therapeutic and surgical procedures are offered to the medical profession in such profusion that the untrained medical man becomes bewildered and the proficient practitioner becomes skeptical. In all this maze of information there must be much tangible and useful information which the medical practitioner and surgeon can and should utilize in his daily practice, but to cull the world's literature with a critical eye and discerning mind is a momentous task; moreover, in order to accomplish this task the worker must have independently acquired much knowledge and experience in order that he may choose and advise wisely. By no means all or even the greater part of stomach and duodenal pathology or disturbed function is based on peptic ulcer, yet peptic ulcer has been the subject of more study than possibly all other specific lesions of the stomach and duodenum; therefore a critical summary of this investigative work is most welcome. The recent work by Hurst and Stewart[1] cannot be alluded to as such a compilation but rather as an elaborate and complete monograph on "Gastric and Duodenal Ulcer." The authors take cognizance of most of the essential work that has been done on the subject and present it in a correlated form which is concise and applicable.

Many chapters have unusual points of interest; the romance of gastric ulcer is presented for those interested in such topics. Stewart, from the viewpoint of a pathologist, gives an unusually lucid description of the pathological anatomy of ulcer. This is followed by Hurst's description of the pathological physiology and an explanation for the cause of pain and tenderness in gastric and duodenal ulcer. This sequence with its conclusions is most convincing. The chapter on radiological investigation is strikingly well illustrated and many significant diagnostic and technical points are presented.

The authors express marked conservatism in recommending direct surgical interference but advocate the removal of all foci of infection and careful and prolonged medical treatment. Their belief is that by far the largest percentage of peptic ulcers will heal and remain healed under this regimen. The presence of occult blood in the stools is stressed, and the authors believe that this finding is a fairly accurate criterion of the healing process of the ulcer. They also offer it as a possible differentiating point between simple ulcer and early carcinoma of the stomach. Here again the chapter on ulcer-cancer is most interesting and illustrates the care and precision which characterizes the preparation of the entire work. In the discussion of jejunal and gastrojejunal ulcer many pertinent points are presented.

The American reader may be doubtful of the possibility of the high percentage of permanent cures from medical treatment but there is a decided question as to whether in America medical treatment is carried out in detail and over the entire period of the patient's life as advocated by Hurst. The reader acquires the impression that the authors hold that the removal of all foci of infection and care in diet during the remainder of the patient's life are the two all important factors in the permanent cure of peptic ulcer.

This monograph of some 500 pages is beautifully illustrated, worded in excellent English, and presents all aspects of peptic ulcer in a thoroughly scientific yet practical manner. It is a credit to the medical profession and a welcome addition to the library of the medical adept. J. A. WOLFER.

THE author states that the purpose of his book[2] is to furnish the student with a correct introduction to the technique of physical examination and diagnosis of the lungs. There is little new material but most of the salient points of chest examination are concisely and systematically placed. There are only sufficient illustrations and hypothetical problems to bring out the more important diagnostic points which are lost to the beginner in the larger books on this subject. The book should be of great help to the interne. M. HERBERT BARKER.

THE volume[3] by Prof. Voltz really constitutes his report as secretary of the subcommittee of the Radiological Commission of the League of Nations, and deals with carcinoma of the uterus and the vagina. This report was made as part of the work of the Sanitary Division of the League of Nations and owed its initiative to the president of the Cancer Commission, Sir George Seaton Buchanan. A foreword is included from the pen of Dr. A. Doederlein, of Munich. The book deals with historical data, technical methods, and final results in the treatment of cancer of the female genital organs, based upon more than three thousand cases treated in the Doederlein Clinic in Munich. Further data are drawn from the work of Dr. J. Heyman, of Stockholm; Dr. A. Lacassagne, of Paris; and Prof. Cl

[1] GASTRIC AND DUODENAL ULCER. By Arthur F. Hurst, M.A., M.D. (Oxon.), F.R.C.P., and Matthew J. Stewart, M.B. (Glasg.), F.R.C.P. Radiological Sections by P. J. Briggs, M.A. (Cantab.), M.R.C.S., L.R.C.P. New York and London: Humphrey Milford, Oxford University Press, 1929.

[2] PROCEDURE IN EXAMINATION OF THE LUNGS; WITH ESPECIAL REFERENCE TO THE DIAGNOSIS OF TUBERCULOSIS. By Arthur F. Kraetzer, M.D. New York: Oxford University Press, 1930.

[3] SONDERBAENDE ZUR STRAHLENTHERAPIE. Vol. XIII—DIE STRAHLENBEHANDLUNG DER WEIBLICHEN GENITALCARCINOME, METHODEN UND ERGEBNISSE. By Professor Dr. Friedrich Voltz. Foreword by Prof. Dr. Albert Doederlein. Berlin: Urban and Schwarzenberg, 1930.

Regaud, of Paris. The book is full of valuable facts regarding both the roentgen and the radium treatment of genital cancer and should stimulate further and more accurate work in the campaign against this disease. JAMES T. CASE.

THE first half of volume VI of Stoeckel's *Handbuch der Gynaekologie*[1] is in keeping with the first volume previously reviewed—it is a most thorough and complete reference book on gynecology, complete in every detail and most profusely and well illustrated. Von Franqué writes the section on the anatomy, histogenesis, and anatomical diagnosis of cervical and uterine carcinoma. The pathology of cervical and uterine carcinoma, hydatid mole, and chorio-epithelioma and endometrioma by Robert Meyer is written in the same careful and painstaking manner that characterizes all of Robert Meyer's writings. Of special and timely interest is his presentation and discussion of all the various theories pertaining to the histogenesis of endometriosis.

Hinselman, of Altona, contributes the section on the etiology, symptomatology, and diagnosis of cervical and uterine carcinoma and of chorioepithelioma. The description of the colposcope developed by the author and the many illustrations of the views of cervical pathology obtained by means of the colposcope are especially valuable.

The same criticisms hold for this volume as for the preceding ones, namely that the work gives promise of being too large for anything other than a library reference work and further too much space is devoted to bibliography—100 pages out of a total of 1,100. This seems out of place in a "Handbuch." RALPH A. REIS.

THE ninth volume of the Oxford *Monographs on Diagnosis and Treatment*[2] is an exceedingly valuable aid to the practitioner in the difficult and common clinical problems raised by abnormal conditions of the blood. Great advances have recently been made, which are thoroughly set forth in this work. The early diagnosis of pernicious anæmia has become more worth while. The details of this diagnosis are described. Certainly a broader study is now necessary for this diagnosis; withholding it until the extreme anæmia is present may do irreparable harm to the spinal cord. The Price-Jones method of studying anisocytosis is illustrated. The unusual leucocyte responses to infection are described in chapters on agranulocytic angina and glandular fever. The typical and atypical leukæmias are given full description. Two features make this work unusually useful, namely, chapters on the blood in systemic diseases and pregnancy, and a full section on the anæmias of childhood by Blackfan and his associates. Every chapter is completed by two or three pages of references, making in all an extensive bibliography on diseases of the blood. The colored illustrations of typical blood smears are perfectly done. PAUL STARR.

LIKE others in the series of Harper's *Medical Monographs*,[3] Norris' monograph on uterine tumors is a concise and well written summary, useful alike to the practitioner and to the student. Norris has presented the salient aspects of the subject in a manner that should appeal to every gynecologist. His discussion of carcinoma is particularly valuable in its accurate and detailed consideration of the factors of predisposition, growth, differential diagnosis, and treatment. An excellent classification of types of tumors, their incidence, and the stages of advancement are given. The book deserves special commendation as a readable, up to date, and instructive description of uterine tumors. MARK T. GOLDSTINE.

WHITE, in his recent book on *Cancer of the Breast*,[4] gives us a clear, concise treatise on the subject. He takes up the fundamentals of anatomy, physiology, and pathology, and deals with them from the standpoint of treatment. The chapters on signs and symptoms and differential diagnosis of tumors of the breast and classification of malignancy, are written with a view to being instructive and practical to the student. Of more than usual interest is the classification, in that the author has given us some detail of the microscopic grading of malignancy by Broders, MacCarty, and Greenough.

The chapters on the roentgen ray and radium therapy are taken up from the standpoint of technique and the application of the principles of treatment as applied to the various types of the disease, with some of the hopes, the limitations, and the indications for the use of this therapy.

The author recommends early recognition and early and thorough removal, and he stresses the principles of Handley in cutting close to the skin without destroying its blood supply, and superficial to the deep fascia.

To the student of surgery, the chapter on types of surgical procedure is of interest in obtaining detailed information relative to modern accepted principles as laid down by prominent general surgeons. The discussion of pathological examination includes a minute detailed consideration from the standpoint of the gross, the microscopic, frozen section, and the Terry method.

[1] HANDBUCH DER GYNAEKOLOGIE. Vol. VI, first half—ANATOMIE UND DIAGNOSTIK DER CARCINOME, DER BINDEGEWEBSGESCHWUELSTE UND MISCHGESCHWUELSTE DES UTERUS, DER BLASENMOLE, UND DES CHORIONEPITHELIOMA MALIGNUM. By Otto von Franqué, H. Hinselman, and Robert Meyer. Munich: J. F. Bergmann, 1930.

[2] OXFORD MONOGRAPHS ON DIAGNOSIS AND TREATMENT. Edited by Henry A. Christian, M.D., Sc.D., LL.D. Vol. IX—THE DIAGNOSIS AND TREATMENT OF DISEASES OF THE BLOOD. By Thomas Ordway, M.D., and L. Whittington Gorham. New York and London: Oxford University Press, 1930.

[3] UTERINE TUMORS. By Charles C. Norris, M.D. New York and London: Harper & Brothers, 1930.

[4] CANCER OF THE BREAST. By William Crawford White, M.D., F.A.C.S. New York and London: Harper & Brothers, 1930.

The book is very instructive. It should be unusually interesting and can be recommended as being of great help to the student, the practitioner, and the general surgeon, and thus fulfills the purpose of the author in presenting a short but rather complete survey of the subject of cancer of the breast.

W. A. HENDRICKS.

THE notes presented in his manual[1] are the result of Reuben Peterson's twenty-five years' experience in conducting and supervising the demonstration course in obstetrics.

The book is well gotten up in typewriter lithographic form with alternating blank pages for the students to take notes. The illustrations, while few, are adequate for the purpose. The book is small, concise, and full of information. The management of the various complications is such that if followed in the average case it would lead to good results.

The book will fill a very useful niche in the teaching of obstetrics and can be recommended to all of the schools as a safe and conservative notebook on the manikin work.

E. L. CORNELL.

THE fact that Dr. Ballenger's book[2] is now in its sixth edition would be enough to recommend it but each edition has improvements and additions over the previous number. The more recent additions have been chapters on broncho-œsophagoscopy by such noted authorities as Chevalier Jackson and Gabrial Tucker. Dr. Ballenger has also added a special chapter dealing with the streptococcus sore throat because he feels that the organism has assumed a rôle of such importance as to justify a more detailed description. The book contains over eleven hundred pages and is printed on good stock with excellent illustrations and clear type. It is a comprehensive one volume treatise on diseases of the ear, nose, and throat, and makes a handy and ready reference besides a good text.

JOHN F. DELPH.

THE seventh edition of Coakley's manual[3] has 672 pages and 13 chapters with 160 engravings and colored plates. The author needs no introduction and his present volume follows in general outline the scheme of his previous manuals. Designed primarily to put into compact form the essentials of diseases of the nose and throat, the author has purposely omitted all controversial subjects and has placed a ready text in the hands of the practitioner. The book is not extensive but contains all essentials necessary to a good textbook.

JOHN F. DELPH.

THE book by Bailey on *Demonstrations of Physical Signs in Clinical Surgery*,[4] makes its appearance in a second revised and enlarged edition. The work is entirely complete in that it covers the physical signs of practically every surgical condition. The book is written in a clear, lucid style which is made even more effective through the use of numerous excellent illustrations. The author has accomplished much more than the modest title of the work would suggest. He not only describes the physical signs and how to apply them, but he actually teaches diagnosis and differential diagnosis of surgical conditions. The student in his clerkship and dispensary days, the interne in his surgical service would find a wealth of practical information to guide him in his formative stage.

GEO. HALPERIN.

[1] A MANUAL FOR THE DEMONSTRATION COURSE IN OBSTETRICS. By Reuben Peterson, A.B., M.D., F.A.C.S. Ann Arbor, Michigan: Edwards Brothers.

[2] DISEASE OF THE NOSE, THROAT, AND EAR; MEDICAL AND SURGICAL. By William L. Ballenger, M.D., F.A.C.S. Revised by Howard Charles Ballenger, M.D., F.A.C.S. 6th ed. rev. Philadelphia: Lea & Febiger, 1930.

[3] A MANUAL OF DISEASES OF THE NOSE AND THROAT. By Cornelius G. Coakley, A.M., M.D., F.A.C.S. 7th ed. rev. Philadelphia: Lea & Febiger, 1930.

[4] DEMONSTRATIONS OF PHYSICAL SIGNS IN CLINICAL SURGERY. 2d rev. ed. By Hamilton Bailey, F.R.C.S. (Eng.). New York: William Wood & Company, 1930.

## BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

OBSTETRICIA CLINICA Y OBSTETRICA SOCIAL. By Doctor Augusto Turenne. Montevideo: Imprenta Nacional, 1930.

A TEXT-BOOK OF GYNECOLOGY. By Arthur Hale Curtis, M.D. Philadelphia and London: W. B. Saunders Company, 1930.

DIE AVERTINNARKOSE IN DER CHIRURGIE. By Prof. Dr. W. Anschuetz, Dr. K. Specht, Priv.-Doz. Dr. Fr. Tiemann. Berlin: Julius Springer, 1930.

EMERGENCY SURGERY. By Hamilton Bailey, F.R.C.S. (Eng.). Vol. I—Abdomen and Pelvis. New York: William Wood and Company, 1930.

GYNAEKOLOGISCHE OPERATIONSLEHRE. By Dr. H. v. Peham, Dr. J. Amreich. Berlin: S. Karger, 1930.

UEBER DAS PROBLEM DER BOESARTIGEN GESCHWUELSTE; EINE EXPERIMENTELLE UND THEORETISCHE UNTERSUCHUNG. 2d ed. By Prof. Dr. Lothar Heidenhain. Berlin: Julius Springer, 1930.

MEDIZINISCHE PRAXIS; SAMMLUNG FUER AERZTLICHE FORTBILDUNG. Edited by L. R. Grote, A. Fromme, K. Warnekros. Vol. IX—Blutung and Fluor. By Prof. Dr. Hans Runge with a foreword by Prof. Dr. Robert Schroeder. Dresden and Leipzig: Theodor Steinkopff, 1930.

DIAGNOSTICS URGENTS; ABDOMEN. By H. Mondor. Paris: Masson et Cie, 1930.

INTRODUCTION TO MEDICAL BIOMETRY AND STATISTICS. By Raymond Pearl. 2d rev. ed. Philadelphia and London: W. B. Saunders Company, 1930.